

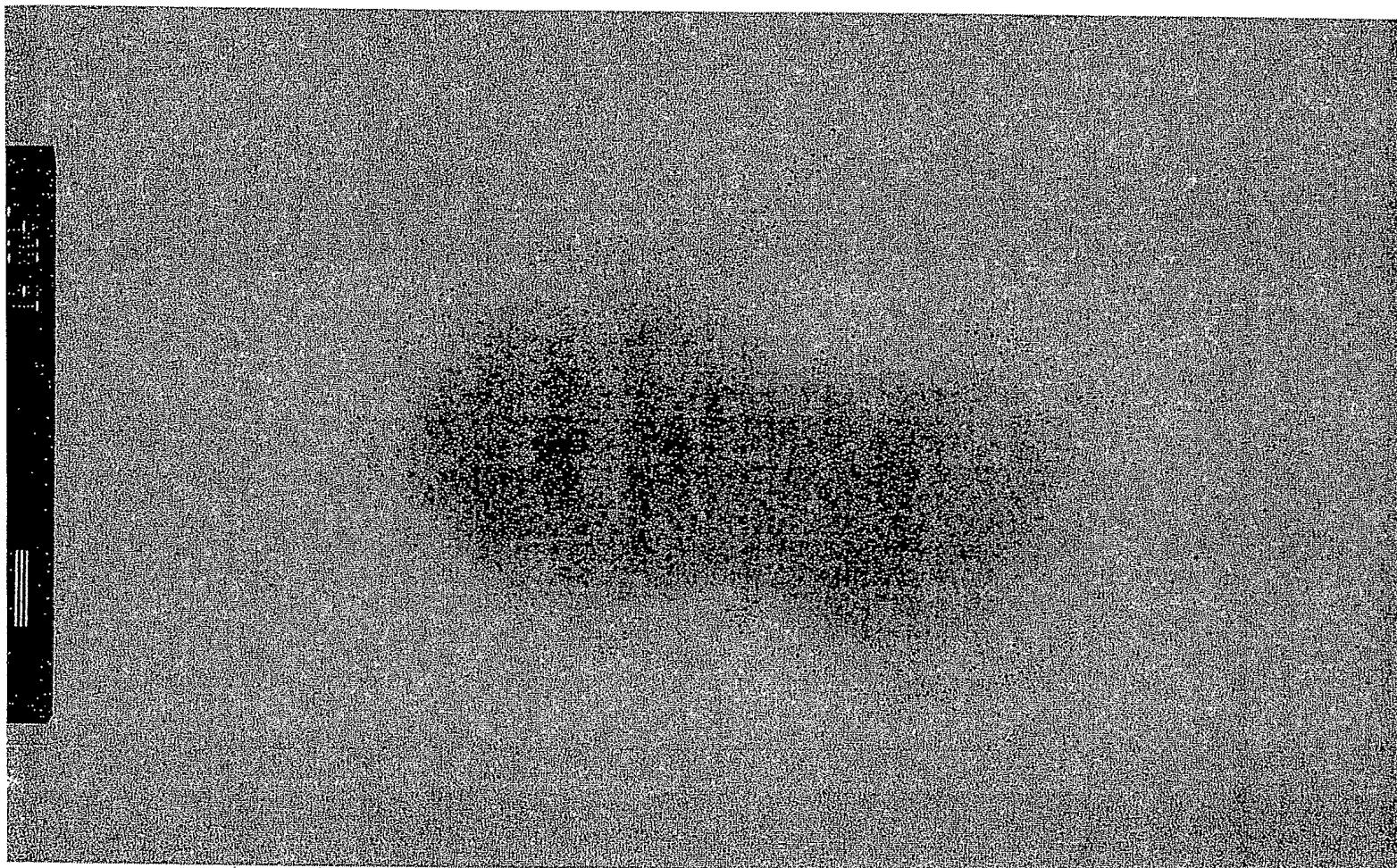
WO 2006/078318

PCT/US2005/027239

321/487

PCT/US2005/027239

Figure 130



WO 2006/078318

PCT/US2005/027239 322/487

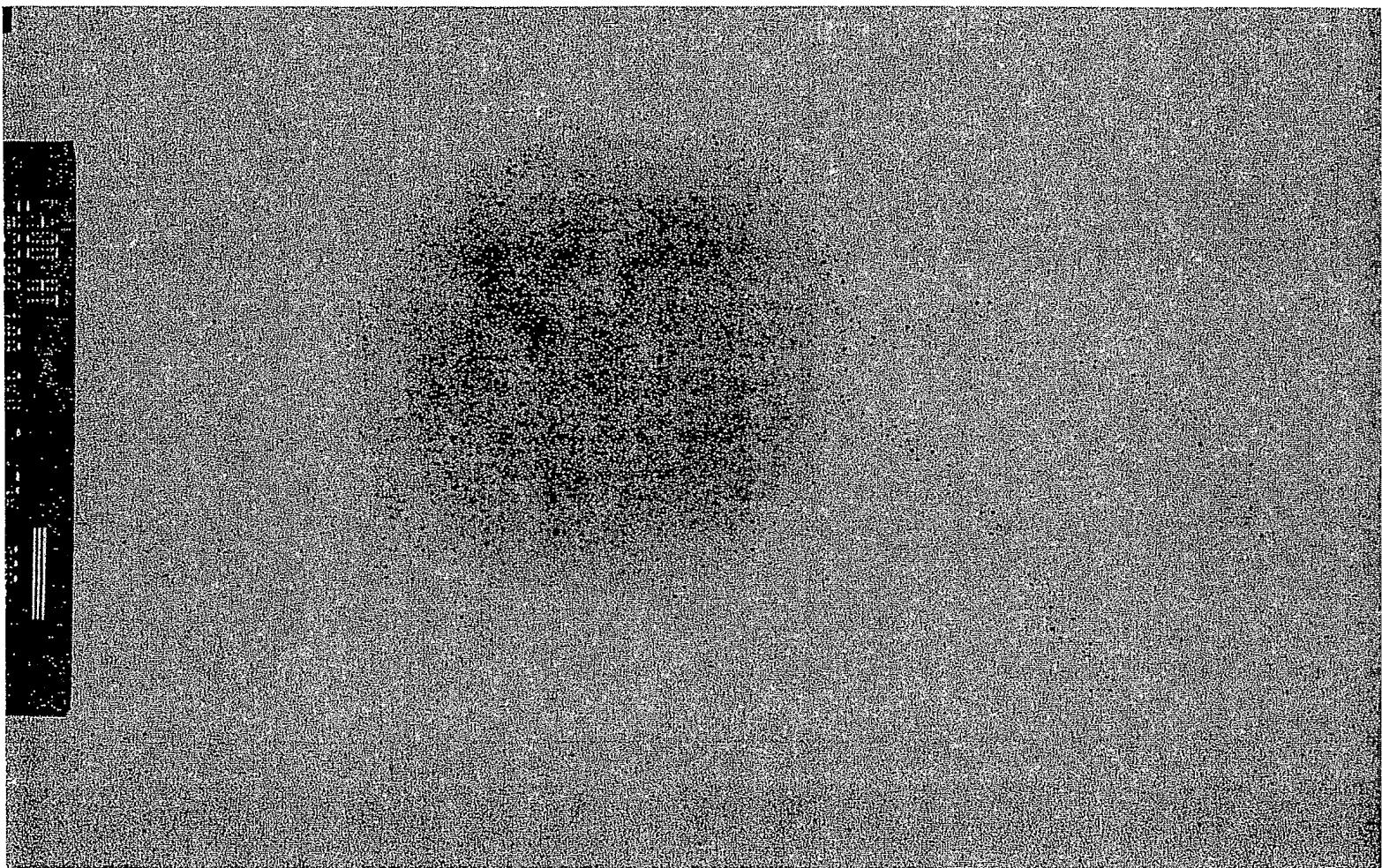
PCT/US2005/027239

Figure 131



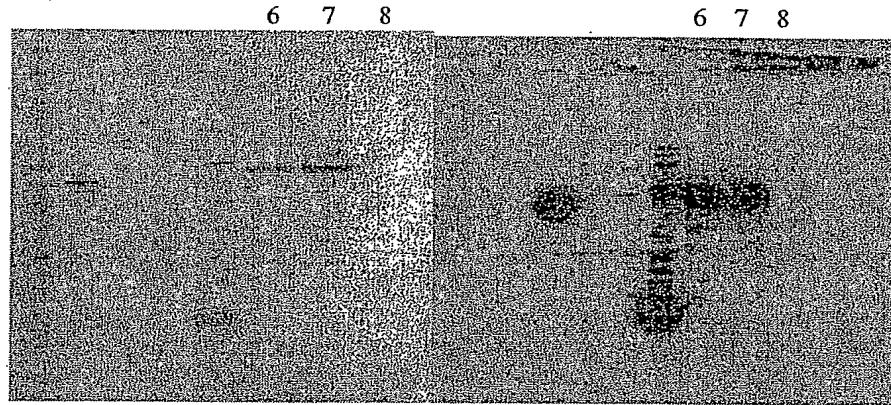
323/487

Figure 132



324/487

Figure 133



A

B

WO 2006/078318

325/487

PCT/US2005/027239

PCT/US2005/027239

Figure 134

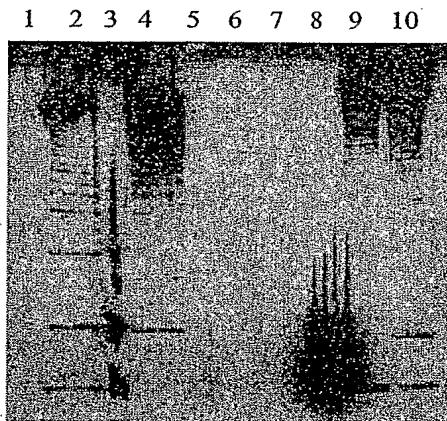
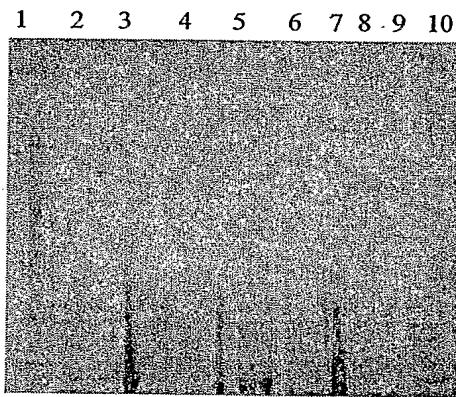


Figure 135



Pilus released by *Lactococcus* sonication

WO 2006/078318

PCT/US2005/27239

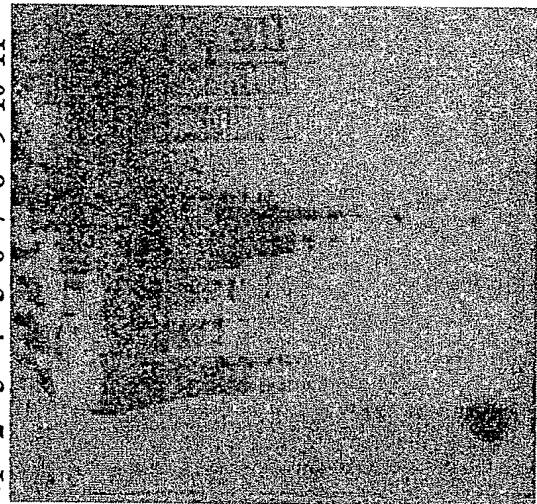
PCT/US2005/027239

327/487

SONICATED

	starting material	pellet	supernatant
1.	MK		
2.	GBS 80 (10 ng)		
3.	<u>L.lactis-AII starting material</u>	(30', 0.2 OD) (not boiled, 0.33 OD)	
4.	L.lactis-AII	(5', 0.33 OD)	
5.	L.lactis-AII	(60' d, 0.33 OD)	
6.	L.lactis-AII	(30', 0.33 OD)	
7.	L.lactis-AII	(not boiled, 2 OD)	
8.	Supernatant		
9.	Supernatant		
10.	Supernatant		
11.	Supernatant		

Figure 136A



α 80

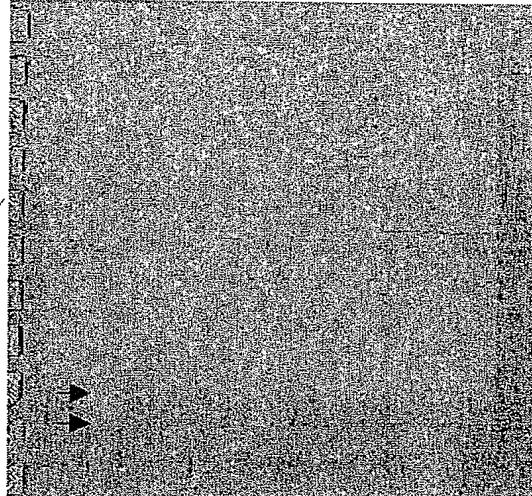


Figure 136B

	starting material		
1.	MK		
2.	L.lactis-AII	(30', 0.33 OD)	
3.	<u>L.lactis-AII starting material</u>	(30', 0.2 OD) (not boiled, 0.33 OD)	
4.	L.lactis-AII	(5', 0.33 OD)	
5.	L.lactis-AII	(60' d, 0.33 OD)	
6.	L.lactis-AII	(30', 0.33 OD)	
7.	L.lactis-AII	(not boiled, 2 OD)	
8.	Supernatant		
9.	Supernatant		
10.	Supernatant		
11.	Supernatant		

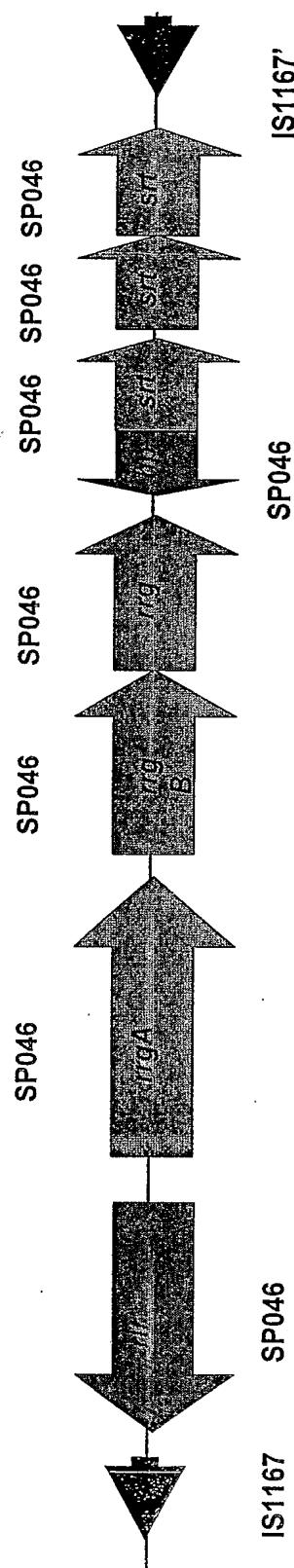


Figure 137

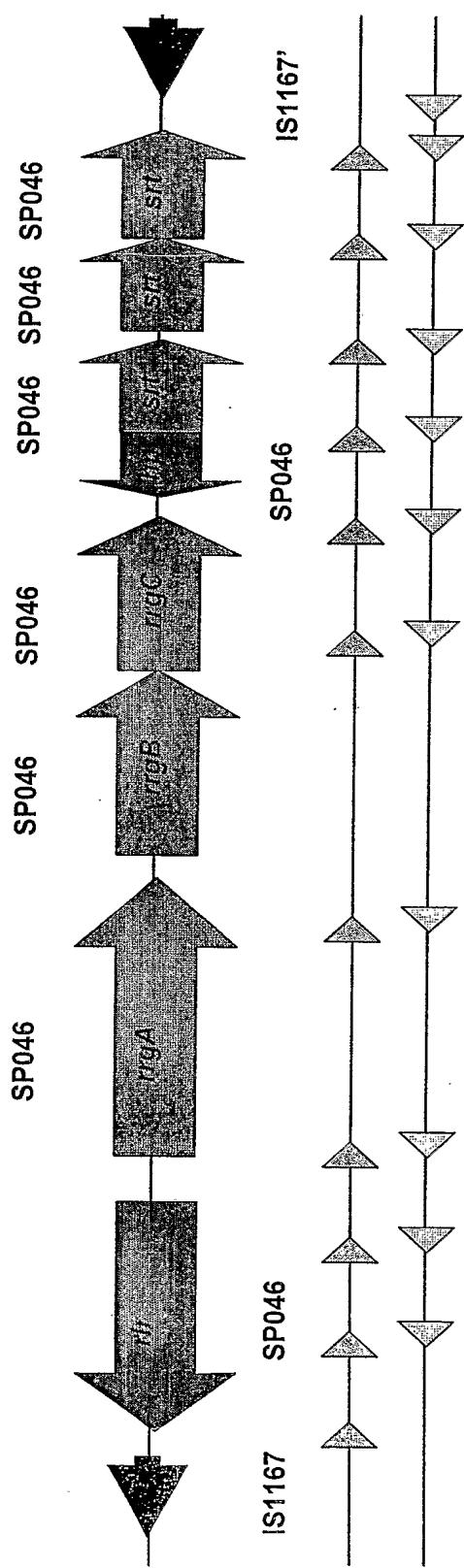
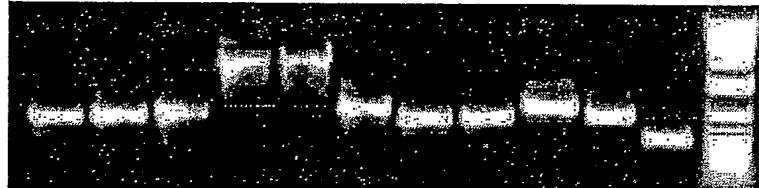


Figure 138

A



TIGR4

B

PCR product	contig_length_TIGR4	overlap
1	754	83
2	759	84
3	847	98
4	2550	99
5	2736	99
6	925	99
7	745	87
8	765	94
9	1008	94
10	802	64
11	461	

Figure 139

PCT/US05/27233 B31/487

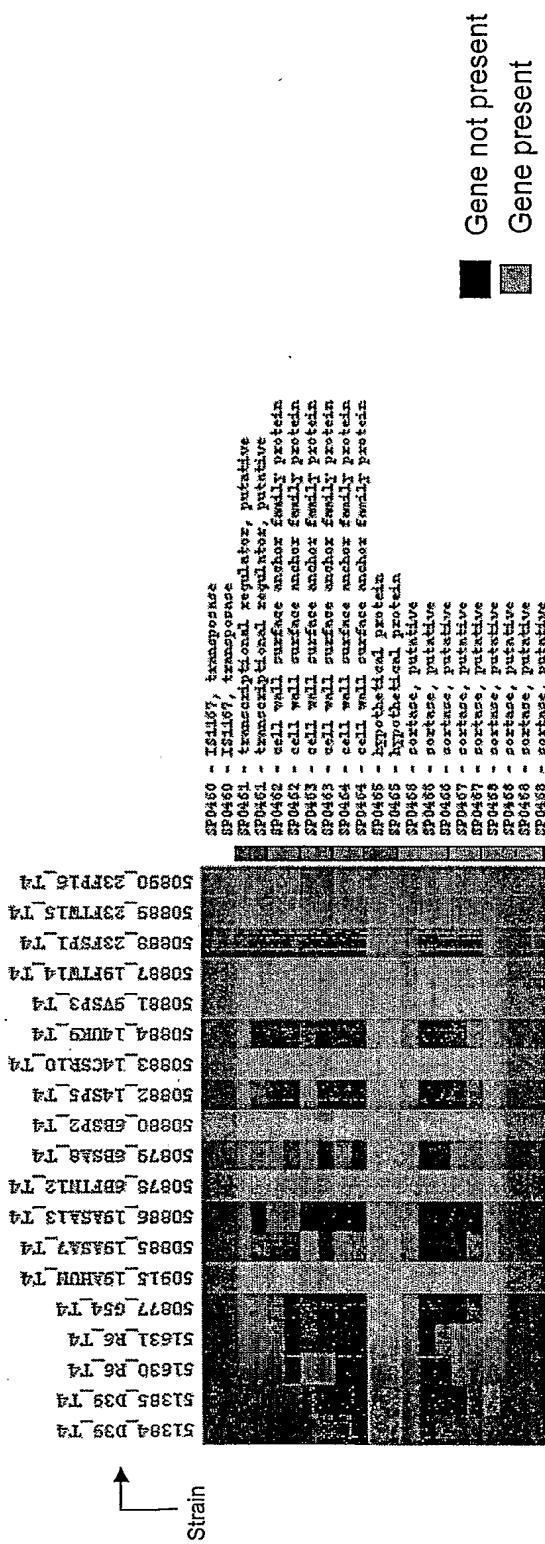


Figure 140

Figure 141A

ORF2_14CSR	MLNKYIEKRITDKITILNILLDIRSIELDELSTLTSQSKSLLSILQELQETFEEELTFN
ORF2_19AH	MLNKYIEKRITDKITILNILLDIRSIELDELSTLTSQSKSLLSILQELQETFEEELTFN
ORF2_19FTW	MLNKYIEKRITDKITILNILLDIRSIELDELSTLTSQSKSLLSILQELQETFEEELTFN
ORF2_23FP	MLNKYIEKRITDKITILNILLDIRSIELDELSTLTSQSKSLLSILQELQETFEEELTFN
ORF2_23FTW	MLNKYIEKRITDKITILNILLDIRSIELDELSTLTSQSKSLLSILQELQETFEEELTFN
ORF2_670	MLNKYIEKRITDKITILNILLDIRSIELDELSTLTSQSKSLLSILQELQETFEEELTFN
ORF2_6BF	MLNKYIEKRITDKITILNILLDIRSIELDELSTLTSQSKSLLSILQELQETFEEELTFN
ORF2_6BSP	MLNKYIEKRITDKITILNILLDIRSIELDELSTLTSQSKSLLSILQELQETFEEELTFN
ORF2_TIGR	MLNKYIEKRITDKITILNILLDIRSIELDELSTLTSQSKSLLSILQELQETFEEELTFN
ORF2_9VSP	MLNKYIEKRITDKITILNILLDIRSIELDELSTLTSQSKSLLSILQELQETFEEELTFN

ORF2_14CSR	LDTQQVQLIEHHSHQTNYYFHQLYNQSTILKILRFFLLOGNQSNEFTQKEYISIATGYR
ORF2_19AH	LDTQQVQLIEHHSHQTNYYFHQLYNQSTILKILRFFLLOGNQSNEFTQKEYISIATGYR
ORF2_19FTW	LDTQQVQLIEHHSHQTNYYFHQLYNQSTILKILRFFLLOGNQSNEFTQKEYISIATGYR
ORF2_23FP	LDTQQVQLIEHHSHQTNYYFHQLYNQSTILKILRFFLLOGNQSNEFTQKEYISIATGYR
ORF2_23FTW	LDTQQVQLIEHHSHQTNYYFHQLYNQSTILKILRFFLLOGNQSNEFTQKEYISIATGYR
ORF2_670	LDTQQVQLIEHHSHQTNYYFHQLYNQSTILKILRFFLLOGNQSNEFTQKEYISIATGYR
ORF2_6BF	LDTQQVQLIEHHSHQTNYYFHQLYNQSTILKILRFFLLOGNQSNEFTQKEYISIATGYR
ORF2_6BSP	LDTQQVQLIEHHSHQTNYYFHQLYNQSTILKILRFFLLOGNQSNEFTQKEYISIATGYR
ORF2_TIGR	LDTQQVQLIEHHSHQTNYYFHQLYNQSTILKILRFFLLOGNQSNEFTQKEYISIATGYR
ORF2_9VSP	LDTQQVQLIEHHSHQTNYYFHQLYNQSTILKILRFFLLOGNQSNEFTQKEYISIATGYR

ORF2_14CSR	VRQKCGLLLRSVGLDLVKNQVVGPEYRIRFLIALLOFHFGIEIYDLDGSMDWVTHMIVQ
ORF2_19AH	VRQKCGLLLRSVGLDLVKNQVVGPEYRIRFLIALLOFHFGIEIYDLDGSMDWVTHMIVQ
ORF2_19FTW	VRQKCGLLLRSVGLDLVKNQVVGPEYRIRFLIALLOFHFGIEIYDLDGSMDWVTHMIVQ
ORF2_23FP	VRQKCGLLLRSVGLDLVKNQVVGPEYRIRFLIALLOFHFGIEIYDLDGSMDWVTHMIVQ
ORF2_23FTW	VRQKCGLLLRSVGLDLVKNQVVGPEYRIRFLIALLOFHFGIEIYDLDGSMDWVTHMIVQ
ORF2_670	VRQKCGLLLRSVGLDLVKNQVVGPEYRIRFLIALLOFHFGIEIYDLDGSMDWVTHMIVQ
ORF2_6BF	VRQKCGLLLRSVGLDLVKNQVVGPEYRIRFLIALLOFHFGIEIYDLDGSMDWVTHMIVQ
ORF2_6BSP	VRQKCGLLLRSVGLDLVKNQVVGPEYRIRFLIALLOFHFGIEIYDLDGSMDWVTHMIVQ
ORF2_TIGR	VRQKCGLLLRSVGLDLVKNQVVGPEYRIRFLIALLOFHFGIEIYDLDGSMDWVTHMIVQ
ORF2_9VSP	VRQKCGLLLRSVGLDLVKNQVVGPEYRIRFLIALLOFHFGIEIYDLDGSMDWVTHMIVQ

ORF2_14CSR	SNSQLSHELLEITPDEYVHFSILVALTWKRREFPLEFPESKFEKLKNLFMYPILMEHCQ
ORF2_19AH	SNSQLSHELLEITPDEYVHFSILVALTWKRREFPLEFPESKFEKLKNLFMYPILMEHCQ
ORF2_19FTW	SNSQLSHELLEITPDEYVHFSILVALTWKRREFPLEFPESKFEKLKNLFMYPILMEHCQ
ORF2_23FP	SNSQLSHELLEITPDEYVHFSILVALTWKRREFPLEFPESKFEKLKNLFMYPILMEHCQ
ORF2_23FTW	SNSQLSHELLEITPDEYVHFSILVALTWKRREFPLEFPESKFEKLKNLFMYPILMEHCQ
ORF2_670	SNSQLSHELLEITPDEYVHFSILVALTWKRREFPLEFPESKFEKLKNLFMYPILMEHCQ
ORF2_6BF	SNSQLSHELLEITPDEYVHFSILVALTWKRREFPLEFPESKFEKLKNLFMYPILMEHCQ
ORF2_6BSP	SNSQLSHELLEITPDEYVHFSILVALTWKRREFPLEFPESKFEKLKNLFMYPILMEHCQ
ORF2_TIGR	SNSQLSHELLEITPDEYVHFSILVALTWKRREFPLEFPESKFEKLKNLFMYPILMEHCQ
ORF2_9VSP	SNSQLSHELLEITPDEYVHFSILVALTWKRREFPLEFPESKFEKLKNLFMYPILMEHCQ

ORF2_14CSR	TYLEPHANMTFTQEELDYIFLVYCSANSSFSKDKWNQEKKTHTIQLILQHTRGKHLLSKF
ORF2_19AH	TYLEPHANMTFTQEELDYIFLVYCSANSSFSKDKWNQEKKTHTIQLILQHTRGKHLLSKF
ORF2_19FTW	TYLEPHANMTFTQEELDYIFLVYCSANSSFSKDKWNQEKKTHTIQLILQHTRGKHLLSKF
ORF2_23FP	TYLEPHANMTFTQEELDYIFLVYCSANSSFSKDKWNQEKKTHTIQLILQHTRGKHLLSKF
ORF2_23FTW	TYLEPHANMTFTQEELDYIFLVYCSANSSFSKDKWNQEKKTHTIQLILQHTRGKHLLSKF
ORF2_670	TYLEPHANMTFTQEELDYIFLVYCSANSSFSKDKWNQEKKTHTIQLILQHTRGKHLLSKF
ORF2_6BF	TYLEPHANMTFTQEELDYIFLVYCSANSSFSKDKWNQEKKTHTIQLILQHTRGKHLLSKF
ORF2_6BSP	TYLEPHANMTFTQEELDYIFLVYCSANSSFSKDKWNQEKKTHTIQLILQHTRGKHLLSKF
ORF2_TIGR	TYLEPHANMTFTQEELDYIFLVYCSANSSFSKDKWNQEKKTHTIQLILQHTRGKHLLSKF
ORF2_9VSP	TYLEPHANMTFTQEELDYIFLVYCSANSSFSKDKWNQEKKTHTIQLILQHTRGKHLLSKF

PCT/US05/23399

Figure 141B

ORF2_14CSR	KNILGNDISNSLSFLTALTFLTRTFLFGLQNLVPYNNYEHYGIESDKPLYHISKAIVQE
ORF2_19AH	KNILGNDISNSLSFLTALTFLTRTFLFGLQNLVPYNNYEHYGIESDKPLYHISKAIVQE
ORF2_19FTW	KNILGNDISNSLSFLTALTFLTRTFLFGLQNLVPYNNYEHYGIESDKPLYHISKAIVQE
ORF2_23FP	KNILGNDISNSLSFLTALTFLTRTFLFGLQNLVPYNNYEHYGIESDKPLYHISKAIVQE
ORF2_23FTW	KNILGNDISNSLSFLTALTFLTRTFLFGLQNLVPYNNYEHYGIESDKPLYHISKAIVQE
ORF2_670	KNILGNDISNSLSFLTALTFLTRTFLFGLQNLVPYNNYEHYGIESDKPLYHISKAIVQE
ORF2_6BF	KNILGNDISNSLSFLTALTFLTRTFLFGLQNLVPYNNYEHYGIESDKPLYHISKAIVQE
ORF2_6BSP	KNILGNDISNSLSFLTALTFLTRTFLFGLQNLVPYNNYEHYGIESDKPLYHISKAIVQE
ORF2_TIGR	KNILGNDISNSLSFLTALTFLTRTFLFGLQNLVPYNNYEHYGIESDKPLYHISKAIVQE
ORF2_9VSP	KNILGNDISNSLSFLTALTFLTRTFLFGLQNLVPYNNYEHYGIESDKPLYHISKAIVQE

ORF2_14CSR	WMTEQKIEGVIDQHRLYLFSLYLTETIFSSLPAIPIFIILNNQADVNLIKSIIILRNFTDK
ORF2_19AH	WMTEQKIEGVIDQHRLYLFSLYLTETIFSSLPAIPIFIILNNQADVNLIKSIIILRNFTDK
ORF2_19FTW	WMTEQKIEGVIDQHRLYLFSLYLTETIFSSLPAIPIFIILNNQADVNLIKSIIILRNFTDK
ORF2_23FP	WMTEQKIEGVIDQHRLYLFSLYLTETIFSSLPAIPIFIILNNQADVNLIKSIIILRNFTDK
ORF2_23FTW	WMTEQKIEGVIDQHRLYLFSLYLTETIFSSLPAIPIFIILNNQADVNLIKSIIILRNFTDK
ORF2_670	WMTEQKIEGVIDQHRLYLFSLYLTETIFSSLPAIPIFIILNNQADVNLIKSIIILRNFTDK
ORF2_6BF	WMTEQKIEGVIDQHRLYLFSLYLTETIFSSLPAIPIFIILNNQADVNLIKSIIILRNFTDK
ORF2_6BSP	WMTEQKIEGVIDQHRLYLFSLYLTETIFSSLPAIPIFIILNNQADVNLIKSIIILRNFTDK
ORF2_TIGR	WMTEQKIEGVIDQHRLYLFSLYLTETIFSSLPAIPIFIILNNQADVNLIKSIIILRNFTDK
ORF2_9VSP	WMTEQKIEGVIDQHRLYLFSLYLTETIFSSLPAIPIFIILNNQADVNLIKSIIILRNFTDK

ORF2_14CSR	VASVTGYNILISPSSSEEHLTEPLIITTKEYLPYVKKQYPKGKHHFLTIALDLHVSQQR
ORF2_19AH	VASVTGYNILISPSSSEEHLTEPLIITTKEYLPYVKKQYPKGKHHFLTIALDLHVSQQR
ORF2_19FTW	VASVTGYNILISPSSSEEHLTEPLIITTKEYLPYVKKQYPKGKHHFLTIALDLHVSQQR
ORF2_23FP	VASVTGYNILISPSSSEEHLTEPLIITTKEYLPYVKKQYPKGKHHFLTIALDLHVSQQR
ORF2_23FTW	VASVTGYNILISPSSSEEHLTEPLIITTKEYLPYVKKQYPKGKHHFLTIALDLHVSQQR
ORF2_670	VASVTGYNILISPSSSEEHLTEPLIITTKEYLPYVKKQYPKGKHHFLTIALDLHVSQQR
ORF2_6BF	VASVTGYNILISPSSSEEHLTEPLIITTKEYLPYVKKQYPKGKHHFLTIALDLHVSQQR
ORF2_6BSP	VASVTGYNILISPSSSEEHLTEPLIITTKEYLPYVKKQYPKGKHHFLTIALDLHVSQQR
ORF2_TIGR	VASVTGYNILISPSSSEEHLTEPLIITTKEYLPYVKKQYPKGKHHFLTIALDLHVSQQR
ORF2_9VSP	VASVTGYNILISPSSSEEHLTEPLIITTKEYLPYVKKQYPKGKHHFLTIALDLHVSQQR

ORF2_14CSR	LIYQTIVDIRKEAFDKRVAMIAKKAHYLL
ORF2_19AH	LIYQTIVDIRKEAFDKRVAMIAKKAHYLL
ORF2_19FTW	LIYQTIVDIRKEAFDKRVAMIAKKAHYLL
ORF2_23FP	LIYQTIVDIRKEAFDKRVAMIAKKAHYLL
ORF2_23FTW	LIYQTIVDIRKEAFDKRVAMIAKKAHYLL
ORF2_670	LIYQTIVDIRKEAFDKRVAMIAKKAHYLL
ORF2_6BF	LIYQTIVDIRKEAFDKRVAMIAKKAHYLL
ORF2_6BSP	LIYQTIVDIRKEAFDKRVAMIAKKAHYLL
ORF2_TIGR	LIYQTIVDIRKEAFDKRVAMIAKKAHYLL
ORF2_9VSP	LIYQTIVDIRKEAFDKRVAMIAKKAHYLL

Figure 142A

PETUSOS 22239

Figure 142B

Figure 142C

PCTZUG05X22239

Figure 143A

Figure 143B

PCT/US05/22239

Figure 143C

ORF4_6BF
ORF4_6BSP
ORF4_670
ORF4_14CSR
ORF4_19AH
ORF4_23FP
ORF4_23FTW
ORF4_19FTW
ORF4_9VSP
ORF4_TIGR

AKIDD-VEFVVGAGSWNQG--EFNYLKDVQKNDATVVNNKKITIPOTGGIGTIIFAV
AKIDD-VEFVVGAGSWNQG--EFNYLKDVQKNDATVVNNKKITIPOTGGIGTIIFAV
AKIDD-VEFVVGAGSWNQG--EFNYLKDVQKNDATVVNNKKITIPOTGGIGTIIFAV
AKIDD-VEFVVGAGSWNQG--EFNYLKDVQKNDATVVNNKKITIPOTGGIGTIIFAV
AKIDD-VEFVVGAGSWNQG--EFNYLKDVQKNDATVVNNKKITIPOTGGIGTIIFAV
AKIDD-VEFVVGAGSWNQG--EFNYLKDVQKNDATVVNNKKITIPOTGGIGTIIFAV
AKIDD-VEFVVGAGSWNQG--EFNYLKDVQKNDATVVNNKKITIPOTGGIGTIIFAV
AKIDD-VEFVVGAGSWNQG--EFNYLKDVQKNDATVVNNKKITIPOTGGIGTIIFAV
AKLGD-VKFEVVGAGSWNQG--DFNYLKDVQKNDATVVNNKKITIPOTGGIGTIIFAV
ALLTSRQKFEVTATSYSATGQGIEYTAGSGKDDATVVNNKKITIPOTGGIGTIIFAV
ALLTSRQKFEVTATSYSATGQGIEYTAGSGKDDATVVNNKKITIPOTGGIGTIIFAV
ALLTSRQKFEVTATSYSATGQGIEYTAGSGKDDATVVNNKKITIPOTGGIGTIIFAV

ORF4_6BF
ORF4_6BSP
ORF4_670
ORF4_14CSR
ORF4_19AH
ORF4_23FP
ORF4_23FTW
ORF4_19FTW
ORF4_9VSP
ORF4_TIGR

AGAAIMGIAVYAYVKNNKDEDQLA
AGAAIMGIAVYAYVKNNKDEDQLA
AGAAIMGIAVYAYVKNNKDEDQLA
AGAAIMGIAVYAYVKNNKDEDQLA
AGAAIMGIAVYAYVKNNKDEDQLA
AGAVIMGIAVYAYVKNNKDEDQLA
AGAVIMGIAVYAYVKNNKDEDQLA
AGAVIMGIAVYAYVKNNKDEDQLA
AGAVIMGIAVYAYVKNNKDEDQLA
AGAAIMGIAVYAYVKNNKDEDQLA

PC T/LIS05/E272239

Figure 144A

ORF5_6BSP	-----MTMQMQMISMIRIFFVMAFCFLSVWGAHAHQQAQEDHTLVLQLENYQEV
ORF5_TIGR	-----MTMQMQMISMIRIFFVMAFCFLSVWGAHAHQQAQEDHTLVLQLENYQEV
ORF5_6BF	-----MTMQMQMISMIRIFFVMAFCFLSVWGAHAHQQAQEDHTLVLQLENYQEV
ORF5_670	-----MTMQMQMISMIRIFFVMAFCFLSVWGAHAHQQAQEDHTLVLQLENYQEV
ORF5_19AH	-----MTMQMQMISMIRIFFVMAFCFLSVWGAHAHQQAQEDHTLVLQLENYQEV
ORF5_14CSR	-----MTMQMQMISMIRIFFVMAFCFLSVWGAHAHQQAQEDHTLVLQLENYQEV
ORF5_19FTW	-----MTMQMQMISMIRIFFVMAFCFLSVWGAHAHQQAQEDHTLVLQLENYQEV
ORF5_23FTW	-----MTMQMQMISMIRIFFVMAFCFLSVWGAHAHQQAQEDHTLVLQLENYQEV
ORF5_9VSP	-----MTMQMQMISMIRIFFVMAFCFLSVWGAHAHQQAQEDHTLVLQLENYQEV
ORF5_23FP	-----MTMQMQMISMIRIFFVMAFCFLSVWGAHAHQQAQEDHTLVLQLENYQEV *****
ORF5_6BSP	VSQLPSPRDGHRLQWVKLDDSYSYDDRVQIVRDLHSWDENKLSSFKKTSFEMTFLENQIEV
ORF5_TIGR	VSQLPSPRDGHRLQWVKLDDSYSYDDRVQIVRDLHSWDENKLSSFKKTSFEMTFLENQIEV
ORF5_6BF	VSQLPSPRDGHRLQWVKLDDSYSYDDRVQIVRDLHSWDENKLSSFKKTSFEMTFLENQIEV
ORF5_670	VSQLPSPRDGHRLQWVKLDDSYSYDDRVQIVRDLHSWDENKLSSFKKTSFEMTFLENQIEV
ORF5_19AH	VSQLPSPRDGHRLQWVKLDDSYSYDDRVQIVRDLHSWDENKLSSFKKTSFEMTFLENQIEV
ORF5_14CSR	VSQLPSPRDGHRLQWVKLDDSYSYDDRVQIVRDLHSWDENKLSSFKKTSFEMTFLENQIEV
ORF5_19FTW	VSQLPSPRDGHRLQWVKLDDSYSYDDRVQIVRDLHSWDENKLSSFKKTSFEMTFLENQIEV
ORF5_23FTW	VSQLPSPRDGHRLQWVKLDDSYSYDDRVQIVRDLHSWDENKLSSFKKTSFEMTFLENQIEV
ORF5_9VSP	VSQLPSPRDGHRLQWVKLDDSYSYDDRVQIVRDLHSWDENKLSSFKKTSFEMTFLENQIEV
ORF5_23FP	VSQLPSPRDGHRLQWVKLDDSYSYDDRVQIVRDLHSWDENKLSSFKKTSFEMTFLENQIEV *****
ORF5_6BSP	SHIPNGLYYVRSLIQTDAVSYPAEFLFEMTDQTVPLVIVAKKTDTMTTKVKLICKVDQDH
ORF5_TIGR	SHIPNGLYYVRSLIQTDAVSYPAEFLFEMTDQTVPLVIVAKKTDTMTTKVKLICKVDQDH
ORF5_6BF	SHIPNGLYYVRSLIQTDAVSYPAEFLFEMTDQTVPLVIVAKKTDTMTTKVKLICKVDQDH
ORF5_670	SHIPNGLYYVRSLIQTDAVSYPAEFLFEMTDQTVPLVIVAKKTDTMTTKVKLICKVDQDH
ORF5_19AH	SHIPNGLYYVRSLIQTDAVSYPAEFLFEMTDQTVPLVIVAKKTDTMTTKVKLICKVDQDH
ORF5_14CSR	SHIPNGLYYVRSLIQTDAVSYPAEFLFEMTDQTVPLVIVAKKTDTMTTKVKLICKVDQDH
ORF5_19FTW	SHIPNGLYYVRSLIQTDAVSYPAEFLFEMTDQTVPLVIVAKKTDTMTTKVKLICKVDQDH
ORF5_23FTW	SHIPNGLYYVRSLIQTDAVSYPAEFLFEMTDQTVPLVIVAKKTDTMTTKVKLICKVDQDH
ORF5_9VSP	SHIPNGLYYVRSLIQTDAVSYPAEFLFEMTDQTVPLVIVAKKTDTMTTKVKLICKVDQDH
ORF5_23FP	SHIPNGLYYVRSLIQTDAVSYPAEFLFEMTDQTVPLVIVAKKTDTMTTKVKLICKVDQDH *****
ORF5_6BSP	NRLEGVGFKLVSVARDGSEKEVPLIGEYRYSSSGQVGRILYTDKNGEIFVTNLPLGNYRF
ORF5_TIGR	NRLEGVGFKLVSVARDGSEKEVPLIGEYRYSSSGQVGRILYTDKNGEIFVTNLPLGNYRF
ORF5_6BF	NRLEGVGFKLVSVARDGSEKEVPLIGEYRYSSSGQVGRILYTDKNGEIFVTNLPLGNYRF
ORF5_670	NRLEGVGFKLVSVARDGSEKEVPLIGEYRYSSSGQVGRILYTDKNGEIFVTNLPLGNYRF
ORF5_19AH	NRLEGVGFKLVSVARDGSEKEVPLIGEYRYSSSGQVGRILYTDKNGEIFVTNLPLGNYRF
ORF5_14CSR	NRLEGVGFKLVSVARDGSEKEVPLIGEYRYSSSGQVGRILYTDKNGEIFVTNLPLGNYRF
ORF5_19FTW	NRLEGVGFKLVSVARDGSEKEVPLIGEYRYSSSGQVGRILYTDKNGEIFVTNLPLGNYRF
ORF5_23FTW	NRLEGVGFKLVSVARDGSEKEVPLIGEYRYSSSGQVGRILYTDKNGEIFVTNLPLGNYRF
ORF5_9VSP	NRLEGVGFKLVSVARDGSEKEVPLIGEYRYSSSGQVGRILYTDKNGEIFVTNLPLGNYRF
ORF5_23FP	NRLEGVGFKLVSVARDGSEKEVPLIGEYRYSSSGQVGRILYTDKNGEIFVTNLPLGNYRF *****
ORF5_6BSP	KEVEPLAGYAVTTLDTDQVLVDHQLVTITVVNNQKLPRGNVDFMKVDGRTNTSLQGAMFKV
ORF5_TIGR	KEVEPLAGYAVTTLDTDQVLVDHQLVTITVVNNQKLPRGNVDFMKVDGRTNTSLQGAMFKV
ORF5_6BF	KEVEPLAGYAVTTLDTDQVLVDHQLVTITVVNNQKLPRGNVDFMKVDGRTNTSLQGAMFKV
ORF5_670	KEVEPLAGYAVTTLDTDQVLVDHQLVTITVVNNQKLPRGNVDFMKVDGRTNTSLQGAMFKV
ORF5_19AH	KEVEPLAGYAVTTLDTDQVLVDHQLVTITVVNNQKLPRGNVDFMKVDGRTNTSLQGAMFKV
ORF5_14CSR	KEVEPLAGYAVTTLDTDQVLVDHQLVTITVVNNQKLPRGNVDFMKVDGRTNTSLQGAMFKV
ORF5_19FTW	KEVEPLAGYAVTTLDTDQVLVDHQLVTITVVNNQKLPRGNVDFMKVDGRTNTSLQGAMFKV
ORF5_23FTW	KEVEPLAGYAVTTLDTDQVLVDHQLVTITVVNNQKLPRGNVDFMKVDGRTNTSLQGAMFKV
ORF5_9VSP	KEVEPLAGYAVTTLDTDQVLVDHQLVTITVVNNQKLPRGNVDFMKVDGRTNTSLQGAMFKV
ORF5_23FP	KEVEPLAGYAVTTLDTDQVLVDHQLVTITVVNNQKLPRGNVDFMKVDGRTNTSLQGAMFKV *****

PCT/US05/237239

Figure 144B

ORF5_6BSP
 ORF5_TIGR
 ORF5_6BF
 ORF5_670
 ORF5_19AH
 ORF5_14CSR
 ORF5_19FTW
 ORF5_23FTW
 ORF5_9VSP
 ORF5_23FP

MKEESGHYTPVLQNGKEVVVTSGKDGRFRVEGLEYGT
 MKEESGHYTPVLQNGKEVVVTSGKDGRFRVEGLEYGT
 MKEESGHYTPVLQNGKEVVVTSGKDGRFRVEGLEYGT
 MKEESGHYTPVLQNGKEVVVTSGKDGRFRVEGLEYGT
 MKEESGHYTPVLQNGKEVVVTSGKDGRFRVEGLEYGT
 MKEESGHYTPVLQNGKEVVVTSGKDGRFRVEGLEYGT
 MKEENGHYTPVLQNGKEVVVASGKDGRFRVEGLEYGT
 MKEENGHYTPVLQNGKEVVVASGKDGRFRVEGLEYGT
 MKEENGHYTPVLQNGKEVVVASGKDGRFRVEGLEYGT

ORF5_6BSP
 ORF5_TIGR
 ORF5_6BF
 ORF5_670
 ORF5_19AH
 ORF5_14CSR
 ORF5_19FTW
 ORF5_23FTW
 ORF5_9VSP
 ORF5_23FP

GKDTRKELTVVKNNKRPRIDVPTDGEETLYILMLVAILLFGSGYYLTKKPNN
 GKDTRKELTVVKNNKRPRIDVPTDGEETLYILMLVAILLFGSGYYLTKKPNN
 GKDTRKELTVVKNNKRPRIDVPTDGEETLYILMLVAILLFGSGYYLTKKPNN
 GKDTRKELTVVKNNKRPRIDVPTDGEETLYILMLVAILLFGSGYYLTKKPNN
 GKDTRKELTVVKNNKRPRIDVPTDGEETLYILMLVAILLFGSGYYLTKKPNN
 GKDTRKELTVVKNNKRPRIDVPTDGEETLYILMLVAILLFGSGYYLTKKPNN
 GKDTRKELTVVKNNKRPRIDVPTDGEETLYILMLVAILLFGSGYYLTKKTNN
 GKDTRKELTVVKNNKRPRIDVPTDGEETLYILMLVAILLFGSGYYLTKKTNN
 GKDTRKELTVVKNNKRPRIDVPTDGEETLYILMLVAILLFGSGYYLTKKTNN

PCT/US05/27239

Figure 145A

ORF6_23FTW	MLIKMVTKKKQKRNNLLLGVVFIGMAVMAYPLVSRLYYRVESNQQIADFDKEKATLDEA
ORF6_TIGR	MLIKMVTKKKQKRNNLLLGVVFIGMAVMAYPLVSRLYYRVESNQQIADFDKEKATLDEA
ORF6_6BSP	MLIKMVTKKKQKRNNLLLGVVFIGMAVMAYPLVSRLYYRVESNQQIADFDKEKATLDEA
ORF6_6BF	MLIKMVTKKKQKRNNLLLGVVFIGMAVMAYPLVSRLYYRVESNQQIADFDKEKATLDEA
ORF6_670	MLIKMVTKKKQKRNNLLLGVVFIGMAVMAYPLVSRLYYRVESNQQIADFDKEKATLDEA
ORF6_19AH	MLIKMVTKKKQKRNNLLLGVVFIGMAVMAYPLVSRLYYRVESNQQIADFDKEKATLDEA
ORF6_14CSR	MLIKMVTKKKQKRNNLLLGVVFIGMAVMAYPLVSRLYYRVESNQQIADFDKEKATLDEA
ORF6_23FP	MLIKMAKTTKKQKRNNLLLGVVFIGIAVMAYPLVSRLYYRVESENQQIADFDKEKATLDEA
ORF6_9VSP	MLIKMAKTTKKQKRNNLLLGVVFIGIAVMAYPLVSRLYYRVESENQQIADFDKEKATLDEA
ORF6_19FTW	MLIKMAKTTKKQKRNNLLLGVVFIGMAVMAYPLVSRLYYRVESENQQIADFDKEKATLDEA
***** . ***** : ***** : ***** : ***** : ***** : *****	
ORF6_23FTW	DIDERMKLAQAFNDSDLNNVVSGDPWSEEMKKKGRAEYARMLEIHERMGHVEIPVIDVDLP
ORF6_TIGR	DIDERMKLAQAFNDSDLNNVVSGDPWSEEMKKKGRAEYARMLEIHERMGHVEIPVIDVDLP
ORF6_6BSP	DIDERMKLAQAFNDSDLNNVVSGDPWSEEMKKKGRAEYARMLEIHERMGHVEIPVIDVDLP
ORF6_6BF	DIDERMKLAQAFNDSDLNNVVSGDPWSEEMKKKGRAEYARMLEIHERMGHVEIPVIDVDLP
ORF6_670	DIDERMKLAQAFNDSDLNNVVSGDPWSEEMKKKGRAEYARMLEIHERMGHVEIPVIDVDLP
ORF6_19AH	DIDERMKLAQAFNDSDLNNVVSGDPWSEEMKKKGRAEYARMLEIHERMGHVEIPVIDVDLP
ORF6_14CSR	DIDERMKLAQAFNDSDLNNVVSGDPWSEEMKKKGRAEYARMLEIHERMGHVEIPVIDVDLP
ORF6_23FP	DIDERMKLAQAFNDSDLNNVVSGDPWSEEMKKKGRAEYARMLEIHERMGHVEIPAIDVDLP
ORF6_9VSP	DIDERMKLAQAFNDSDLNNVVSGDPWSEEMKKKGRAEYARMLEIHERMGHVEIPAIDVDLP
ORF6_19FTW	DIDERMKLAQAFNDSDLNNVVSGDPWSEEMKKKGRAEYARMLEIHERMGHVEIPAIDVDLP
***** . ***** : ***** : ***** : ***** : *****	
ORF6_23FTW	VYAGTAEEVLQQGAGQLEGTSLPIGGNSTHAVITAHTGLPTAKMFTDLTKLKVGDKFYVH
ORF6_TIGR	VYAGTAEEVLQQGAGHLEGTSLPIGGNSTHAVITAHTGLPTAKMFTDLTKLKVGDKFYVH
ORF6_6BSP	VYAGTAEEVLQQGAGHLEGTSLPIGGNSTHAVITAHTGLPTAKMFTDLTKLKVGDKFYVH
ORF6_6BF	VYAGTAEEVLQQGAGHLEGTSLPIGGNSTHAVITAHTGLPTAKMFTDLTKLKVGDKFYVH
ORF6_670	VYAGTAEEVLQQGAGHLEGTSLPIGGNSTHAVITAHTGLPTAKMFTDLTKLKVGDKFYVH
ORF6_19AH	VYAGTAEEVLQQGAGHLEGTSLPIGGNSTHAVITAHTGLPTAKMFTDLTKLKVGDKFYVH
ORF6_14CSR	VYAGTAEEVLQQGAGHLEGTSLPIGGNSTHAVITAHTGLPTAKMFTDLTKLKVGDKFYVH
ORF6_23FP	VYAGTAEEVLQQGAGHLEGTSLPIGGNSTHAVITAHTGLPTAKMFTDLTKLKVGDKFYVH
ORF6_9VSP	VYAGTAEEVLQQGAGHLEGTSLPIGGNSTHAVITAHTGLPTAKMFTDLTKLKVGDKFYVH
ORF6_19FTW	VYAGTAEEVLQQGAGHLEGTSLPIGGNSTHAVITAHTGLPTAKMFTDLTKLKVGDKFYVH
***** . ***** : ***** : ***** : ***** : *****	
ORF6_23FTW	NIKEVMAYQVDQVKVIEPTNFDDLLIVPGHDYVTLTCTPYMINTHRLLVRGHRIPYVAE
ORF6_TIGR	NIKEVMAYQVDQVKVIEPTNFDDLLIVPGHDYVTLTCTPYMINTHRLLVRGHRIPYVAE
ORF6_6BSP	NIKEVMAYQVDQVKVIEPTNFDDLLIVPGHDYVTLTCTPYMINTHRLLVRGHRIPYVAE
ORF6_6BF	NIKEVMAYQVDQVKVIEPTNFDDLLIVPGHDYVTLTCTPYMINTHRLLVRGHRIPYVAE
ORF6_670	NIKEVMAYQVDQVKVIEPTNFDDLLIVPGHDYVTLTCTPYMINTHRLLVRGHRIPYVAE
ORF6_19AH	NIKEVMAYQVDQVKVIEPTNFDDLLIVPGHDYVTLTCTPYMINTHRLLVRGHRIPYVAE
ORF6_14CSR	NIKEVMAYQVDQVKVIEPTNFDDLLIVPGHDYVTLTCTPYMINTHRLLVRGHRIPYVAE
ORF6_23FP	NIKEVMAYQVDQVKVIEPTNFDDLLIVPGHDYVTLTCTPYMINTHRLLVRGHRIPYVAE
ORF6_9VSP	NIKEVMAYQVDQVKVIEPTNFDDLLIVPGHDYVTLTCTPYMINTHRLLVRGHRIPYVAE
ORF6_19FTW	NIKEVMAYQVDQVKVIEPTNFDDLLIVPGHDYVTLTCTPYMINTHRLLVRGHRIPYVAE
***** . ***** : ***** : ***** : ***** : *****	
ORF6_23FTW	VEEEE FIAANKLSHLYRYLFYVAVGLIVILLWIIRRLRKKKQPEKALKALARKEVKVE
ORF6_TIGR	VEEEE FIAANKLSHLYRYLFYVAVGLIVILLWIIRRLRKKKQPEKALKALARKEVKVE
ORF6_6BSP	VEEEE FIAANKLSHLYRYLFYVAVGLIVILLWIIRRLRKKKQPEKALKALARKEVKVE
ORF6_6BF	VEEEE FIAANKLSHLYRYLFYVAVGLIVILLWIIRRLRKKKQPEKALKALARKEVKVE
ORF6_670	VEEEE FIAANKLSHLYRYLFYVAVGLIVILLWIIRRLRKKKQPEKALKALARKEVKVE
ORF6_19AH	VEEEE FIAANKLSHLYRYLFYVAVGLIVILLWIIRRLRKKKQPEKALKALARKEVKVE
ORF6_14CSR	VEEEE FIAANKLSHLYRYLFYVAVGLIVILLWIIRRLRKKKQPEKALKALARKEVKVE
ORF6_23FP	VEEEE FIAANKLSHLYRYLFYVAVGLIVILLWIIRRLRKKKQSERALKALKEATKEVKVE
ORF6_9VSP	VEEEE FIAANKLSHLYRYLFYVAVGLIVILLWIIRRLRKKKQSERALKALKEATKEVKVE
ORF6_19FTW	VEEEE FIAANKLSHLYRYLFYVAVGLIVILLWIIRRLRKKKQSERALKALKEATKEVKVE
***** . ***** : ***** : ***** : ***** : *****	

Figure 145B

ORF6_23FTW	DGQQ
ORF6_TIGR	DGQQ
ORF6_6BSP	DGQQ
ORF6_6BF	DGQQ
ORF6_670	DGQQ
ORF6_19AH	DGQQ
ORF6_14CSR	DGQQ
ORF6_23FP	DE--
ORF6_9VSP	DE--
ORF6_19FTW	DE-

PCT/US05/27239 344/481

Figure 146

PCT/US05/22239

Figure 147

PCT/JU5005/27239
346/487

RrgA, LPXTG

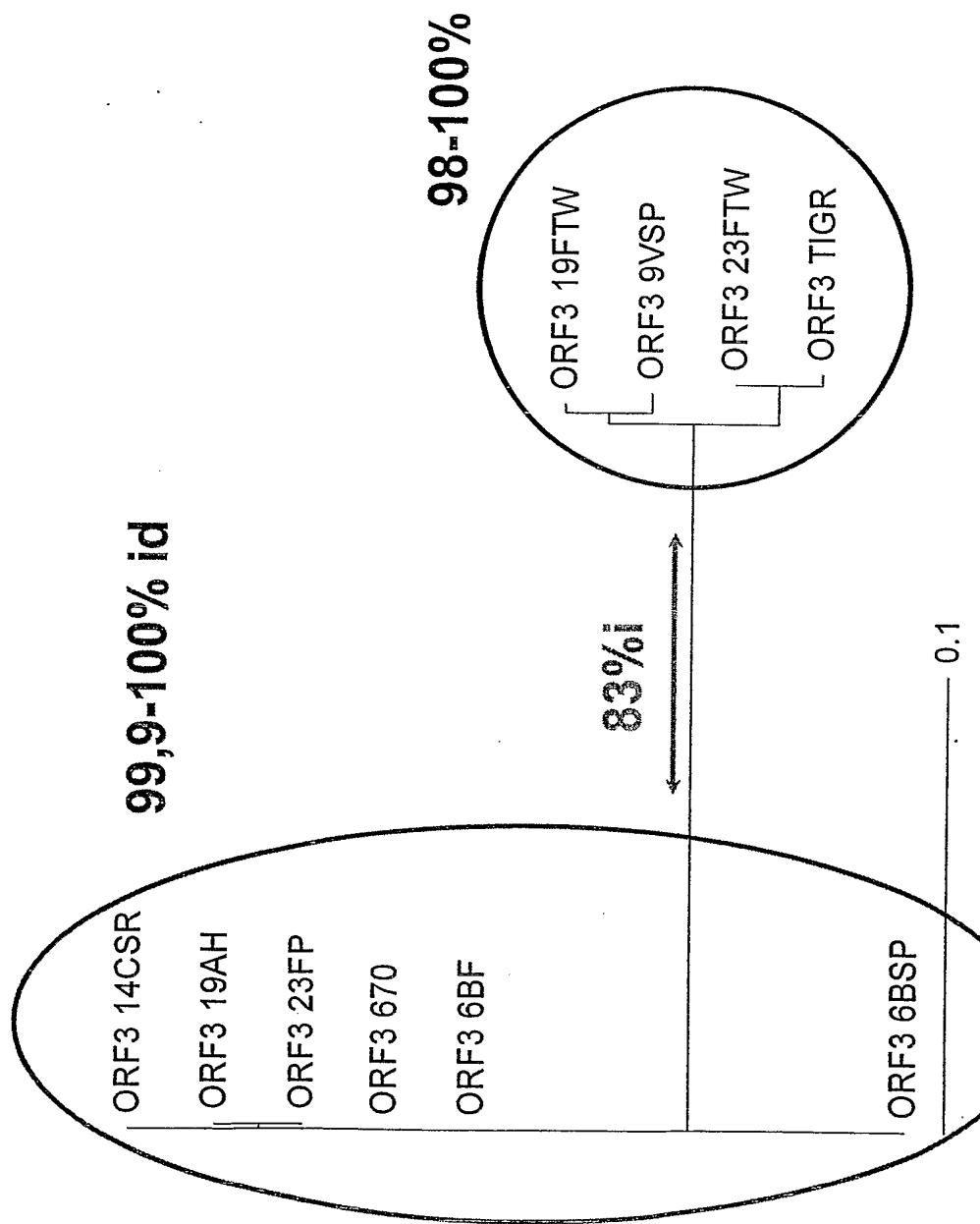
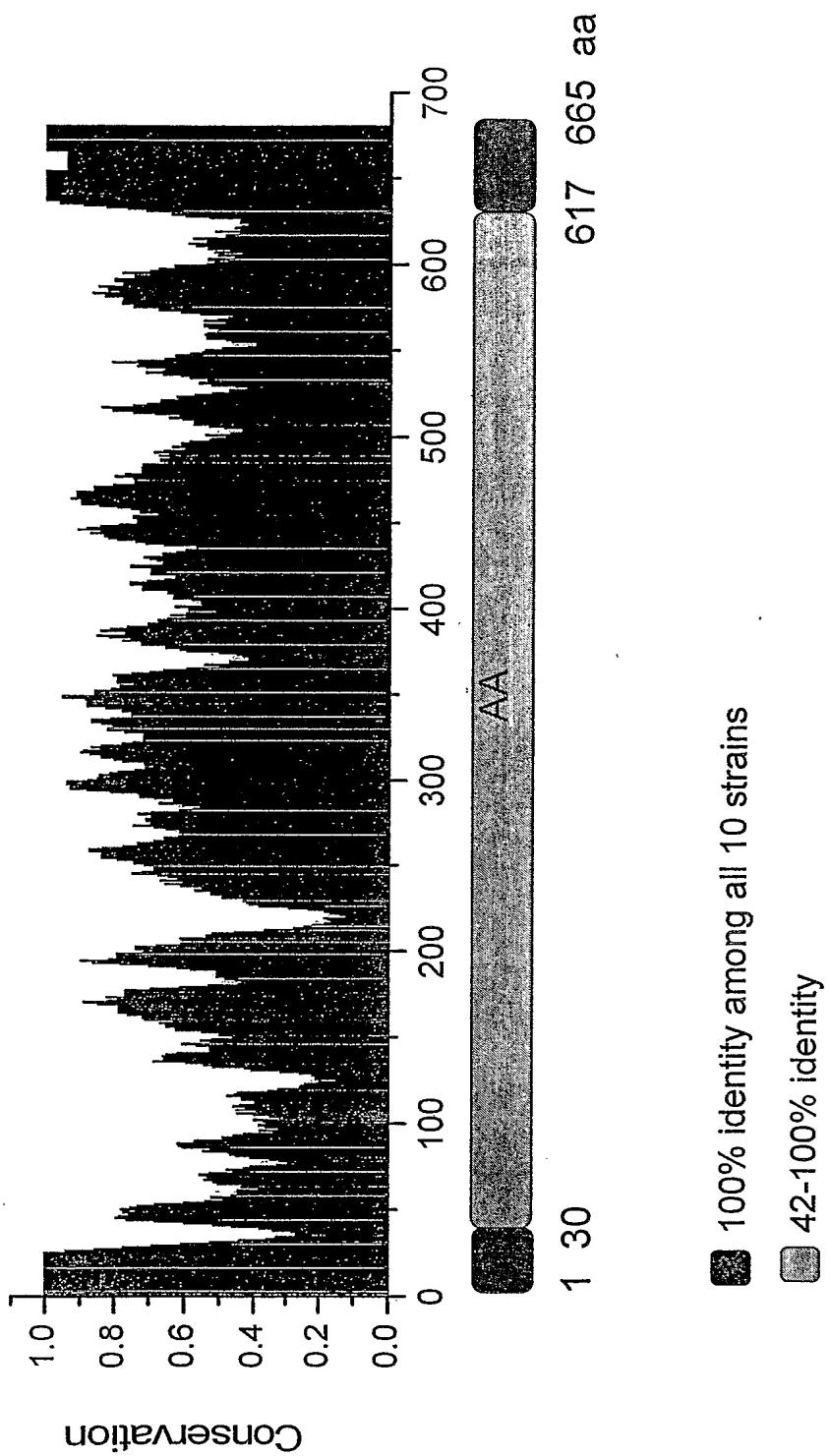


Figure 148



- 100% identity among all 10 strains
- 42-100% identity

Figure 149

A

MLNRETHM/KKKVVKIFQKAVAGLCCISQLTAFSSIVALLA*ETPETSPAIGKVVVIKETGE GGALLGDAVFELKN
 NTDGTTVSQRTEAQATGEAIFSNIKPGTYTLTEAQPPVGYKPKSTKQWTVVEKNGRTTVQGEQVNREE
 ALSDQYPQTGTYPDVQTPYQIKVKYDGSEKNGOHKALNPNPYERVIBEGTLSKRIVQVNNTDDNQYGIEL
 TVSGKTVYEQKDKSVPLDVVILLDNNSNSMSNIRNKNARRAERAAGEATRSLIDKITSDESRVVALVTYAS
 TIEDGTEFTVEKGVADKNGKRLNDSLFWNNYDQTSFTNTKDYSYLKLTNDKNDIVELKNKVPTEAEDHD
 GNRJLMYQFGATFTQKALMKADELTQARQNSOKVIEHTIDGVPTMSYPINFNHATHAPSYQNQLNA
 FFSKSPNKGKDGLLSDFITQATSGEHTIVRGDGQSYQMFTDKTVYEKGAPA AFFPVKPEKYSEMKAAGYAVI
 GDPINGGYIWLNWRESIIAYPFNSNTAKITNHGDPTRWYYNGNIAPDGYDVFTVGIGINGDPGTDEATA
 TSEFMQSISSKPNENYTINVTDITKILEQLNRYFHTIVTEKKSIENGTTIDPMGEJLDLQLGTDGRFDPADYTL
 TANDGSRLENGQAVGGPQNDGGLLKNAKVLYDTTEKRIVTGLYLTGTDEKVTLTLYNVRNLNDEFVSNKFYD
 TNGRTTLHPKEVEQNTVRDFPPKIRDVRYKYPEITISKEKKLGDEFIKVKNNDKPLRGAVFSLQKQHPDYP
 DIYGAIDQONGTYQNVRTGEDGKLTFKNLSDGKYRLEENSEPAGYKFVNKPKVAFQIVNGEVRDVTSIVPQ
 DPAGYEFNTNDKHYTNEPPP~~KREYPRTGIGMLPFYLIGCMMGGVILYTRKHP~~

B

5' cggatcc-gaa-acg-cct-gaa-acc-agt 5' 24mer, 54 %G+C, Tm 62

BamHI

3' ccgcctcagg-aat-agg-itc-att-ggt 3' 27mer, 52 %G+C, Tm 61.6

XbaI

Figure 150

A.

38 862



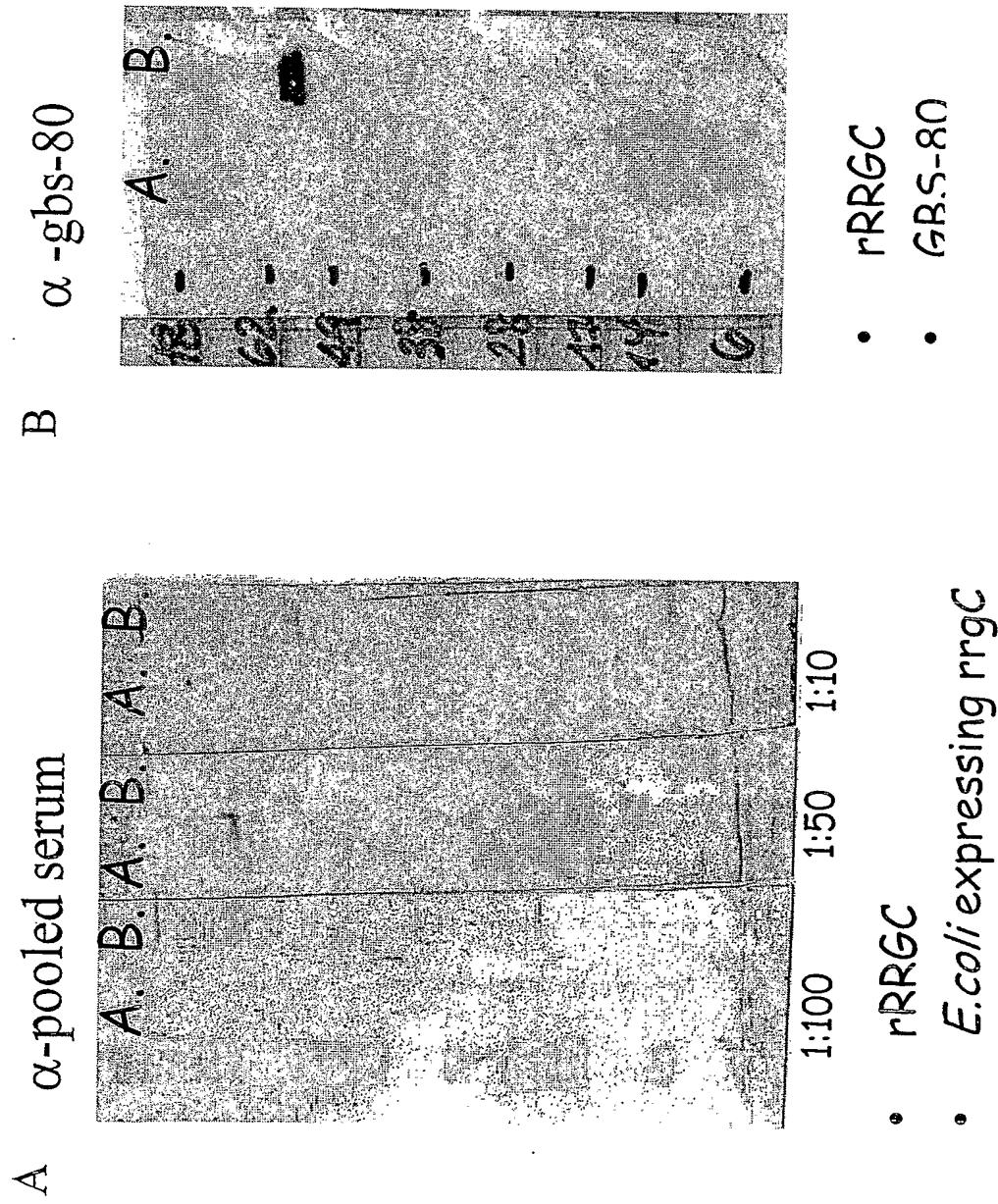
B.



Figure 151

PCT/US2005/027239 350/487

Figure 152



351/487

A

*MKSINKFLTML4ALLTASSLFS*AAATVFAAGTTTSSVTVHKLLATDGDMDKIANELETGNYAGNKVGVLPA
 NAKEIA GVMFWWTNTNNEIDENGQTLGVNIDPQTFLKLSGAMPATAMKKLTSEAEGAKFTANLPAAKYKTY
 EHSLSSTYYVEDGATL TGSKAVPIETELPLINDVVDAHVYPKNTAEAKPKDKDFKGKANPDTPRVDKDTIPVNHQV
 GDVVEYEIVTKP ALANYATANWSDRMTEGLAFNKGTVKVTVDDVALEAGDYALTEVATGFIDLKLTDAGLAK
 VNDQNAEKTVKJISATLNDKAIVEVPESNDVTENYGNNPDHGNTPKPNKPNENGDLTLTKTWVDAATGAPP
 AGAEATFDLVNAQTGKVVQTVTLTTDKNTVTVNGLDKNTTEYKFVERSIGYSADYQEITTAAGEIAVKNWKD
 ENPKPLDPTEPKVVTYGKKFVKVNDKDNRLAGAEFVIANADNAQGYLARKADKVSQEEKQLVYVTTKDALDRAY
 AAYNALTAQQQTQQEKEVKDAQAA YNAAVIAANNAFEWVADKDNEVVKLVSDAQGRFEITGLLAGTY
 YLEETKQPGYALLTSRQKFEVATSYSATGQGIEYTAGSCKDDATKVVNNK KITPQTGGIGTHFAVAGAAI
 MGIAVYAYVKNM KDEDQLA*

B

5' cggatcc-gtt-gca-aca-gtt-ttt 3' 23mer, 52.2% G+C, Tm 60.6

BamHI

5' ccgttcgg-agt-gat-ttt-ttt-gtt-gac 3' 26mer, 44.4% G+C, Tm 61.7

XbaI

Figure 153

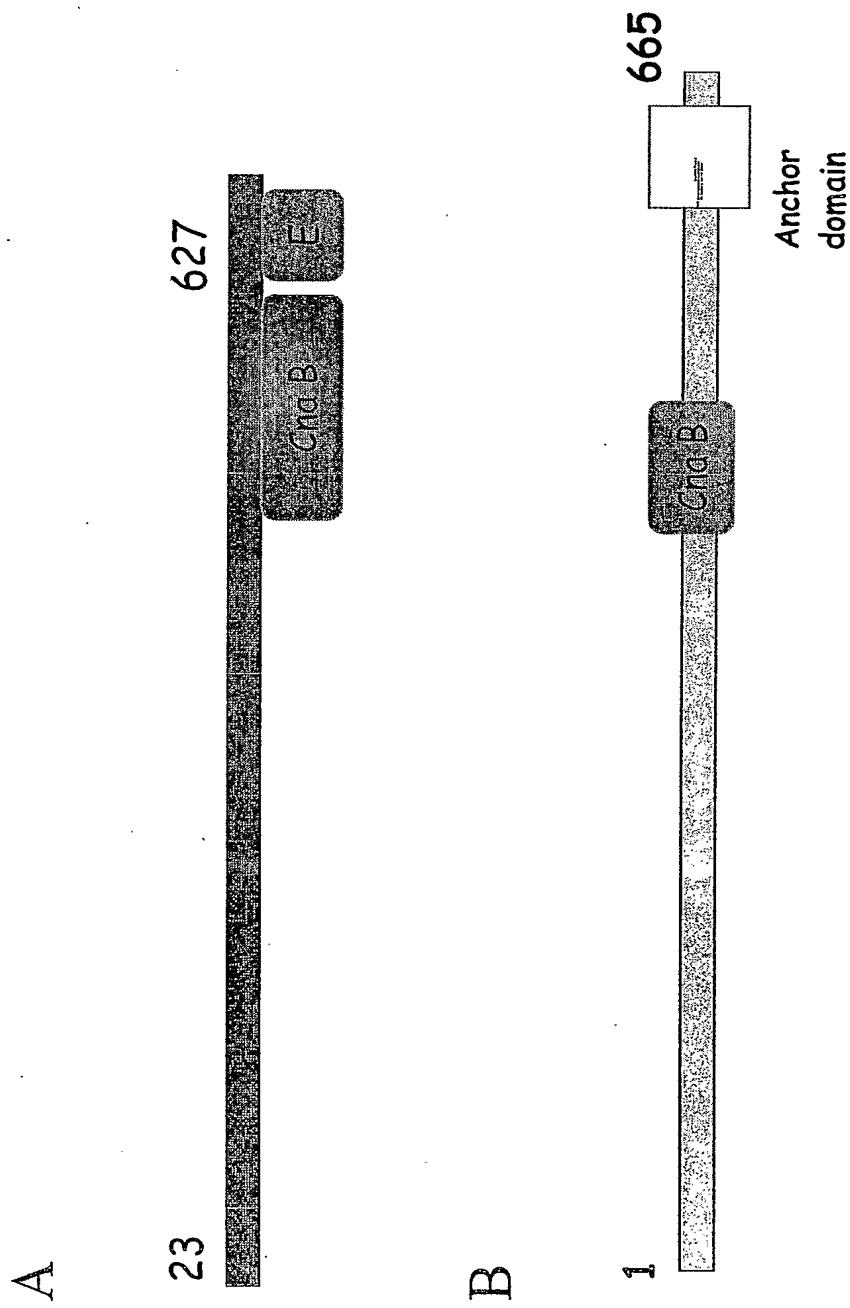
PCT/US05/27239
352/487

Figure 154

PCT/US05/27239
353/487

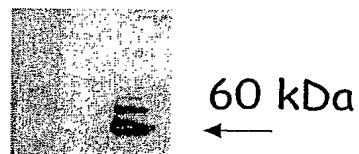


Figure 155

a T
r I
k G D
e R 3 R
r 4 9 6

500 →

290 →

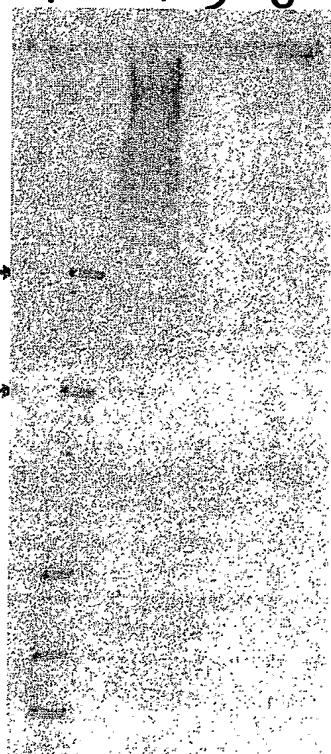


Figure 156

A

*MISRIFVMALCFSLIVWGA*HAYQAQEDHTLVLQLENYQEVVSQLPSRDGHRLQVWKLDDSYS
 YDDRVQIVRDLHSWDENKLSSFEKKTSFEMTFLENQIEVSHPNGLYYVRSIIQTDAVSYPAEFLF
 EMTDQTVEPLIVVAKKTTDKMTIKVKKLKVQDFHNRLEGVGFKLVSVARDVSEKEVPLIGEYRYSSS
 GQVGRRTLYTDKNGEIFVTNLPLGNYRFKEVEPLAGYAVTTLDTDVQLVDHQLVITTVNQKLPRGN
 VDFMKVVDGRTNTSLQGAMFKVMKEESGHYTPVILQNGKEVVVVTSGKDGRFRVEGLYGTYYLWELQ
 APTGYVQLTSPVSFTIGKDTRKELVTVVKNNKRPRRIDVPTGEETLYILMLVAILLFGSGYVLTKKP
 MN*

B

5' cggatcc-cat-gca-gtc-caa-gcg-caa-gaa 21mer, 61% G+C, Tm 60.8
BamHI

5' ccgcctggc-ctt-gtt-att-ttt-aac-ac 27mer, 44% G+C, Tm 58.4
XbaI

Figure 157

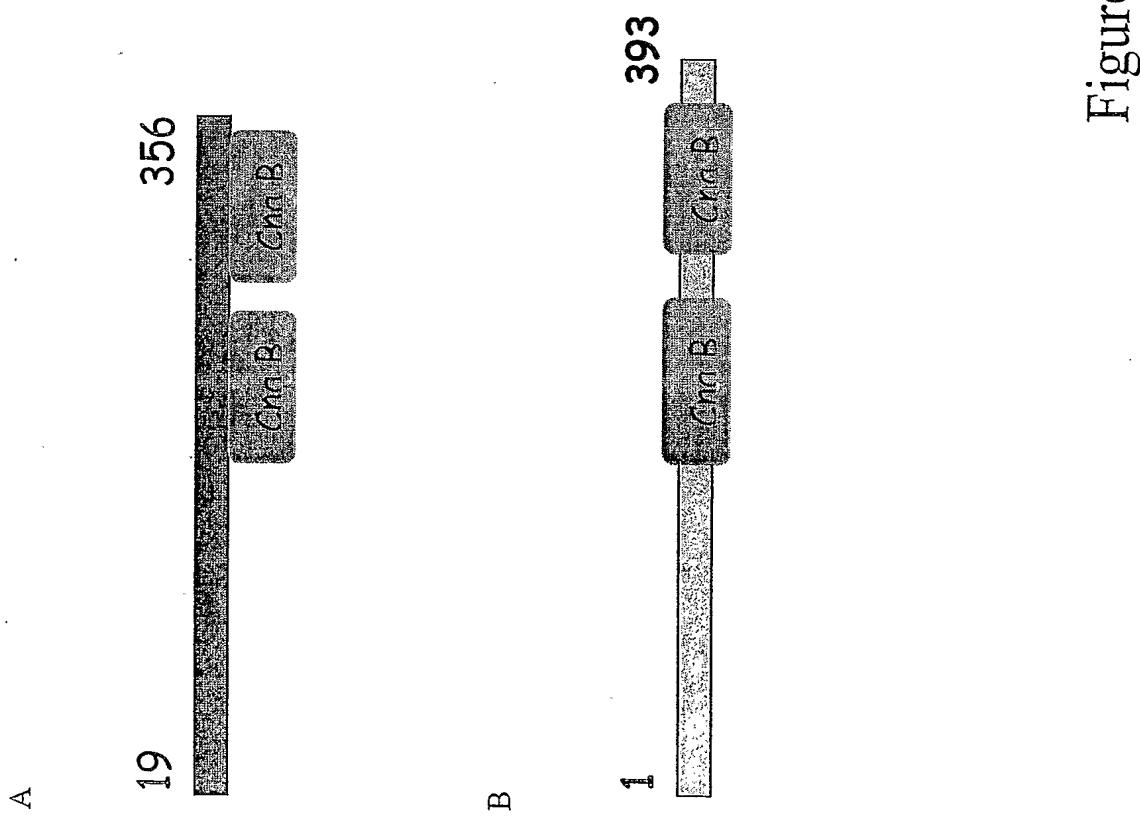


Figure 158

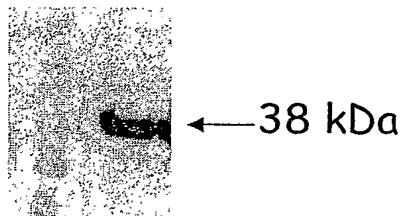


Figure 159

358/487

rr rr rr
g g g
M A B C

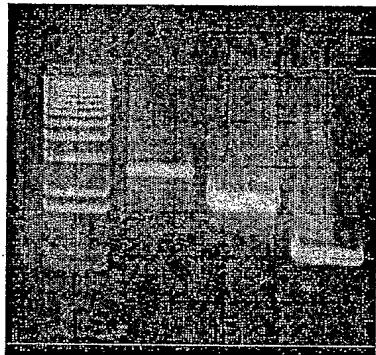
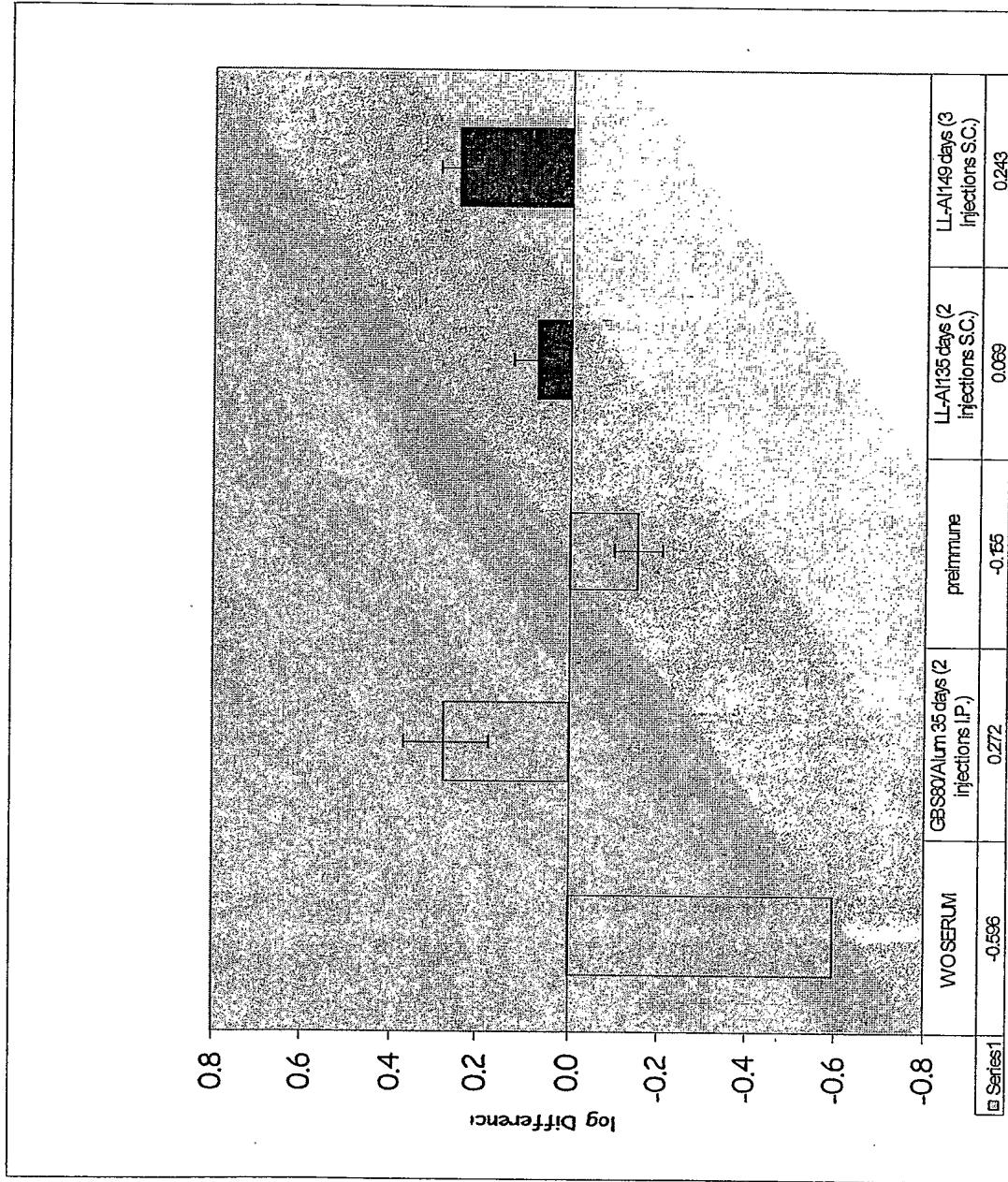


Figure 160

359/487

Figure 161



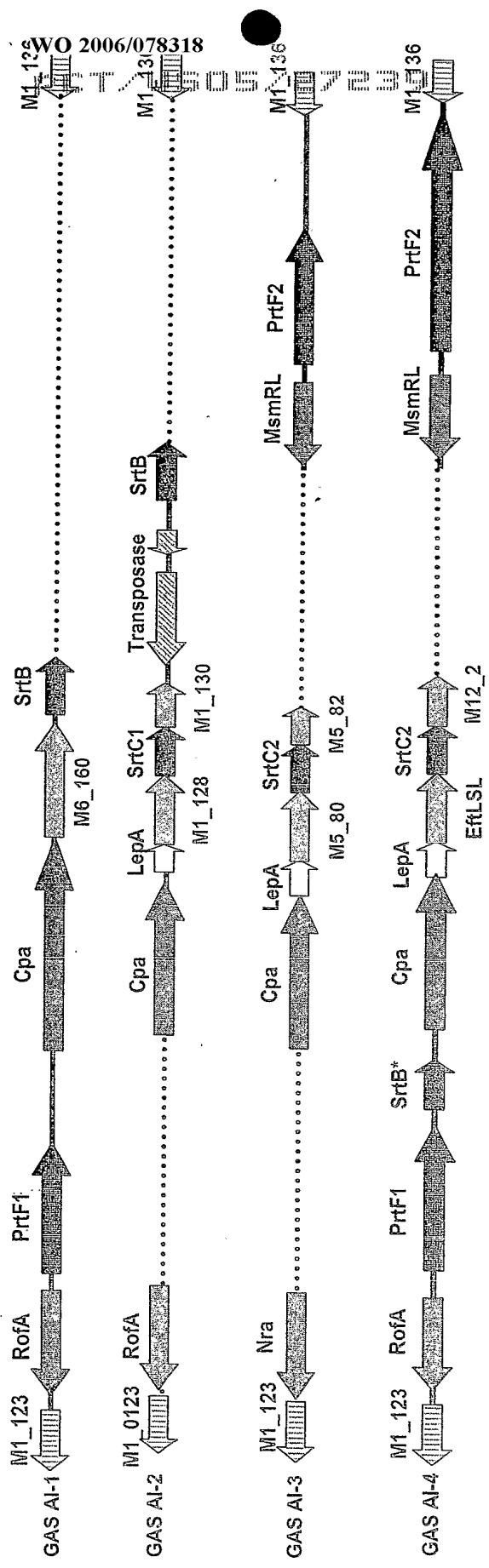
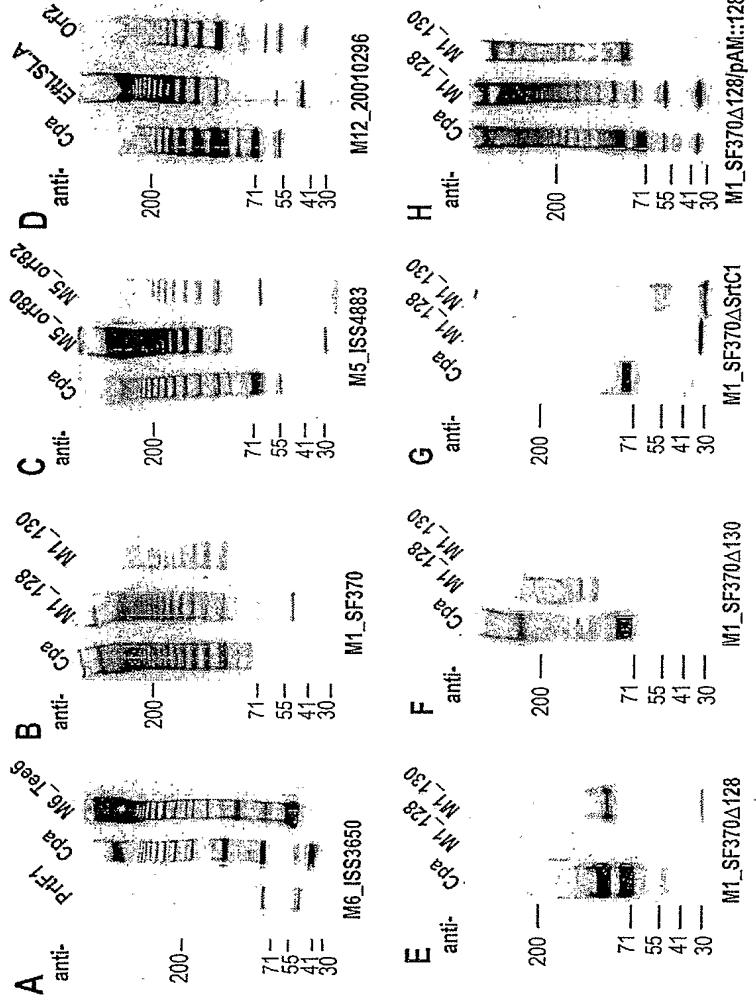
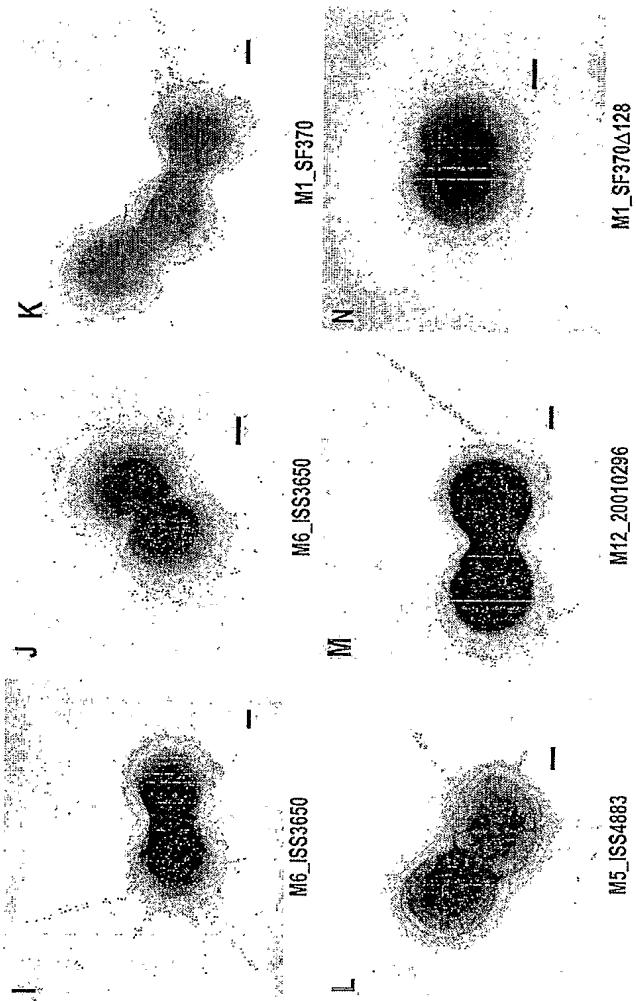


FIGURE 162

PCT/US05/27239 361/487

Figure
163

PCT/US05/27233 362/487

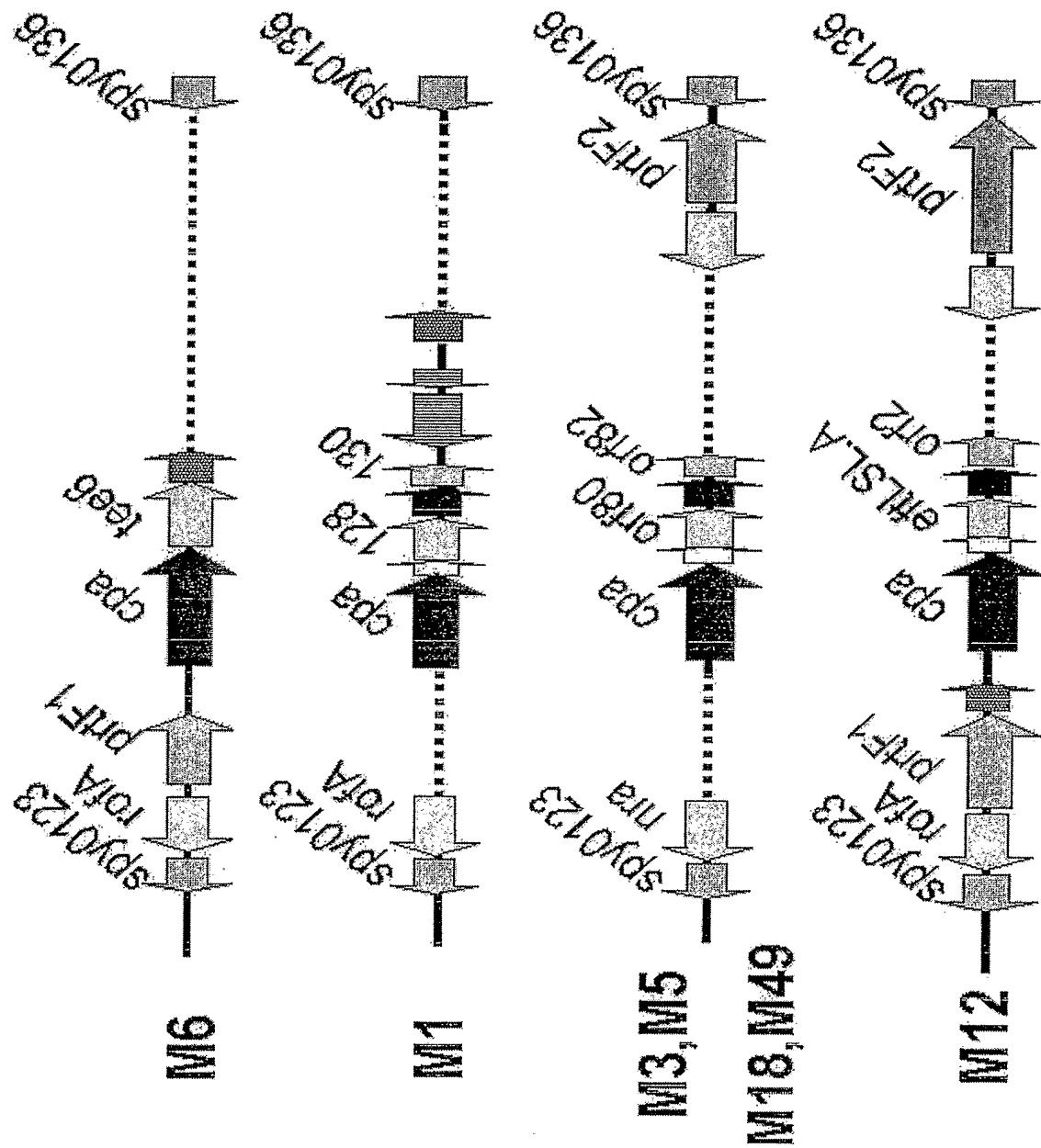


Figure 164

PCT/US05/27239 363/487

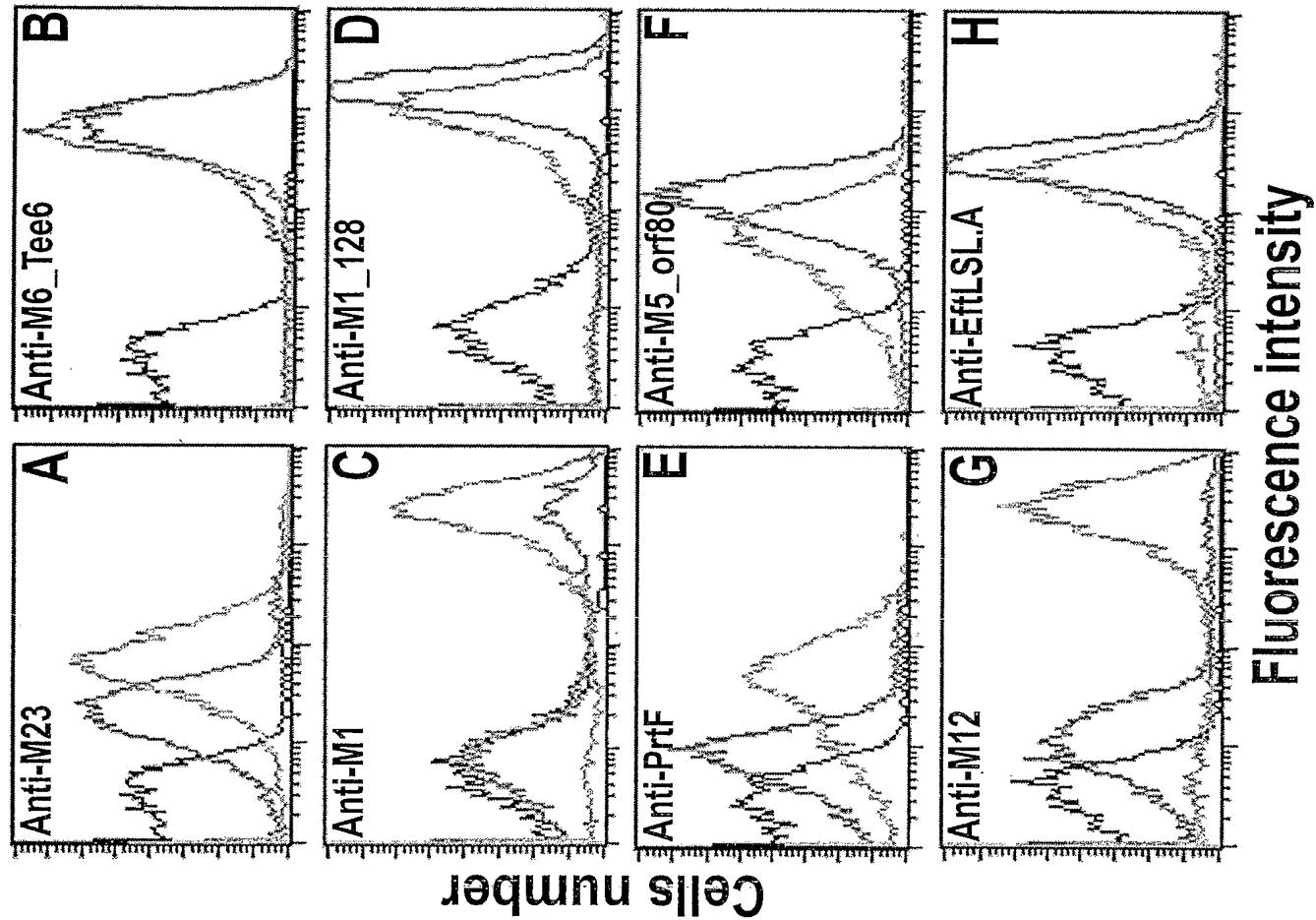


Figure 165

PCT/US05/237239

364/487

Figure

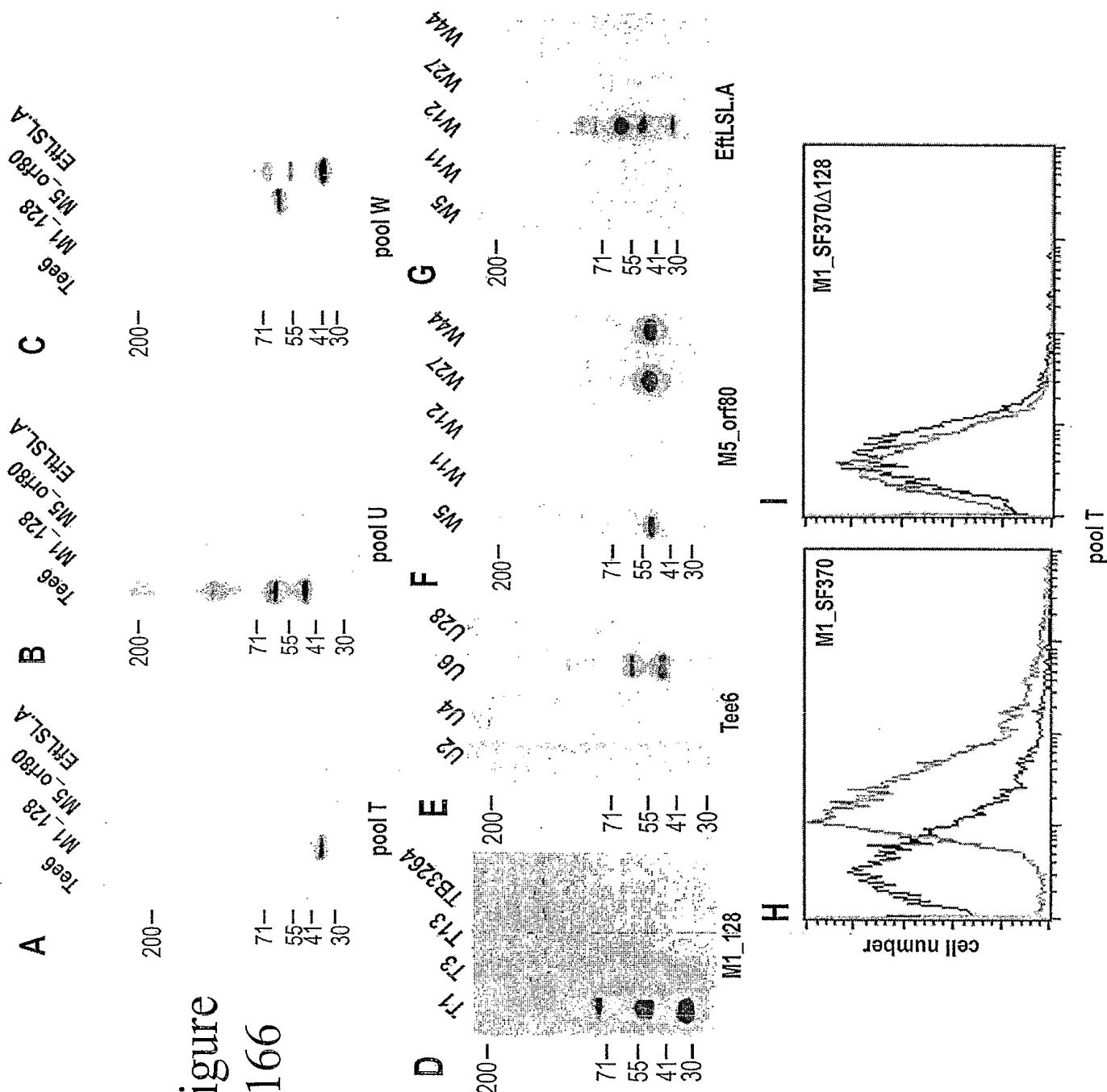


Figure 167

Strain	M-type	PCR						Sequence
		SrtB	SrtC1	SrtC2	MsmRL	SipA2	AI	
2724	6	+	-	-	-	-	1	
2894	6	+	-	-	-	-	1	
3650	6	+	-	-	-	-	1	
5529	6	+	-	-	-	-	1	
Dsm2071	23	+	-	-	-	-	1	+
SF370	1	+	+	-	-	-	2	literature
2580	1	+	+	-	-	-	2	
2913	1	+	+	-	-	-	2	
3280	1	+	+	-	-	-	2	
3348	1	+	+	-	-	-	2	
2719	?	+	+	-	-	-	2	
2721	3	-	-	+	+	+	3	
3040	3	-	-	+	+	+	3	
3135	3	-	-	+	+	+	3	
3776	44 ?	-	-	+	+	+	3	+
4959	77	-	-	+	+	+	3	+
4088	Clinical isolate	-	-	+	+	+	3	
2728	12	+	-	+	+	+	4	
2720	9	+	-	+	+	+	4	+
2727	11	+	-	+	+	+	4	+
4436	28	+	-	+	+	+	4	+
5481	44 ?	+	-	+	+	+	4	+
4538	50	+	-	+	+	+	4	+
3789	78	+	-	+	+	+	4	+
4883	5	■	■	■	■	■	■	
5476	89	+	-	+	+	+	4	
5495	?	+	-	+	+	+	4	
2722	4	-	-	-	-	-	?	
2723	5?	-	-	-	-	-	?	
2725	8	-	-	+	-	-	?	
2726	2	-	-	-	-	-	?	
2634	4	-	-	-	-	-	?	
5531	75	+	+	-	-	-	?	In progress

366/487

Figure 168

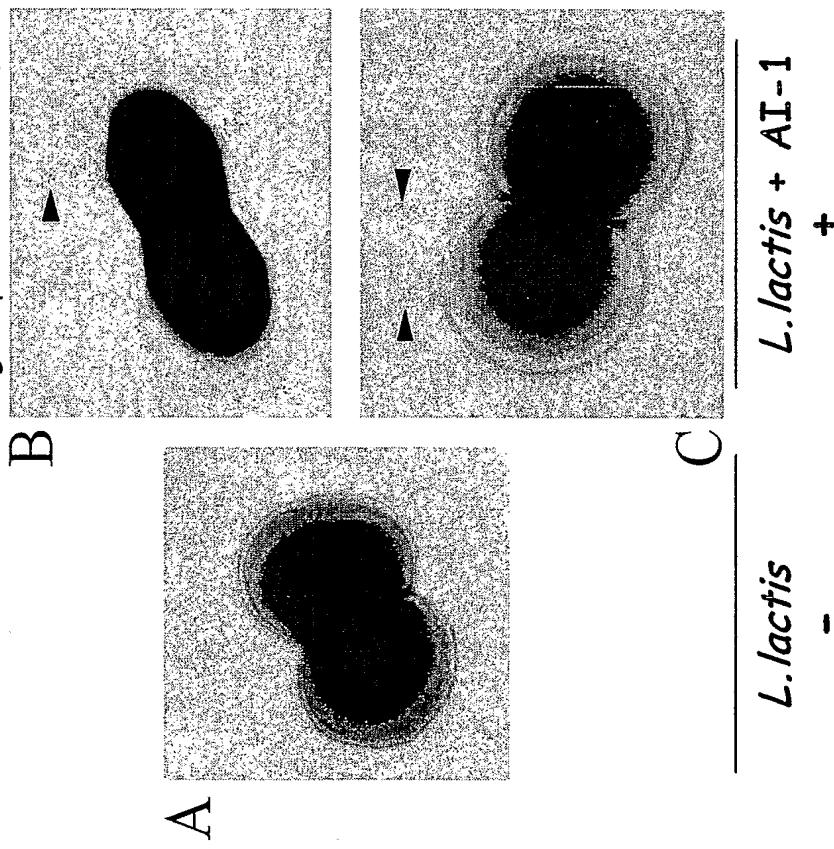
Immuno-electron microscopy(Immunogold Negative Staining,
1° α - 80, 2° α -mouse gold particles 10nm)

Figure 169

*L. lactis**L. lactis + AI-1*

GBS JM9130013

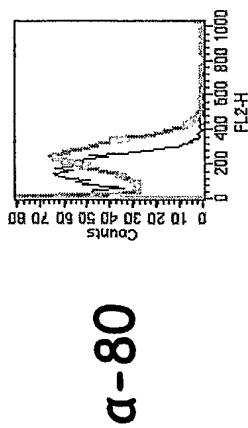
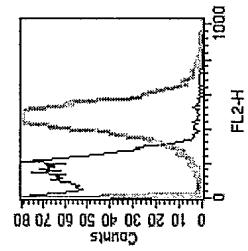
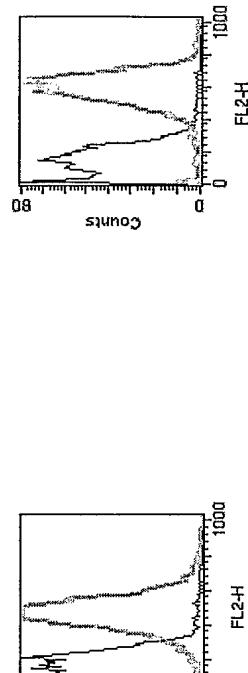
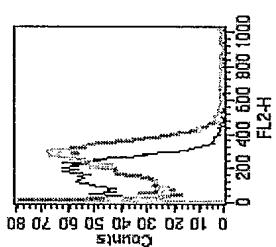
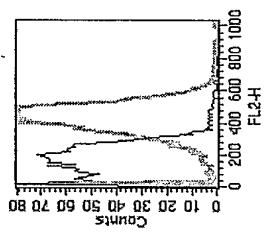
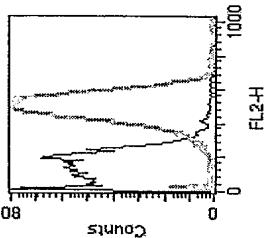
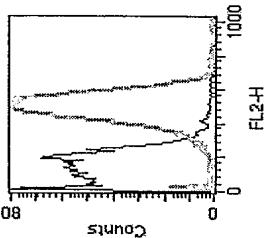
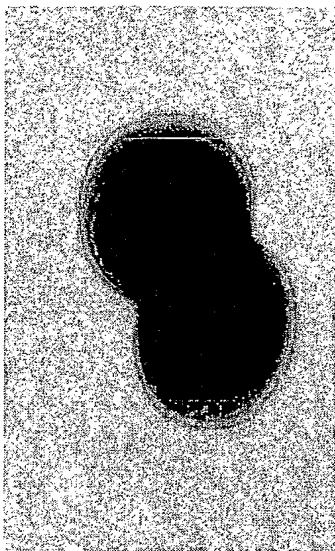
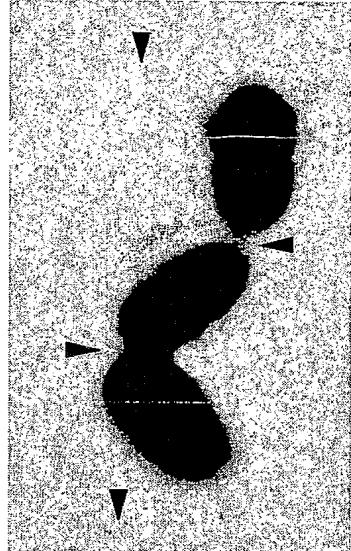
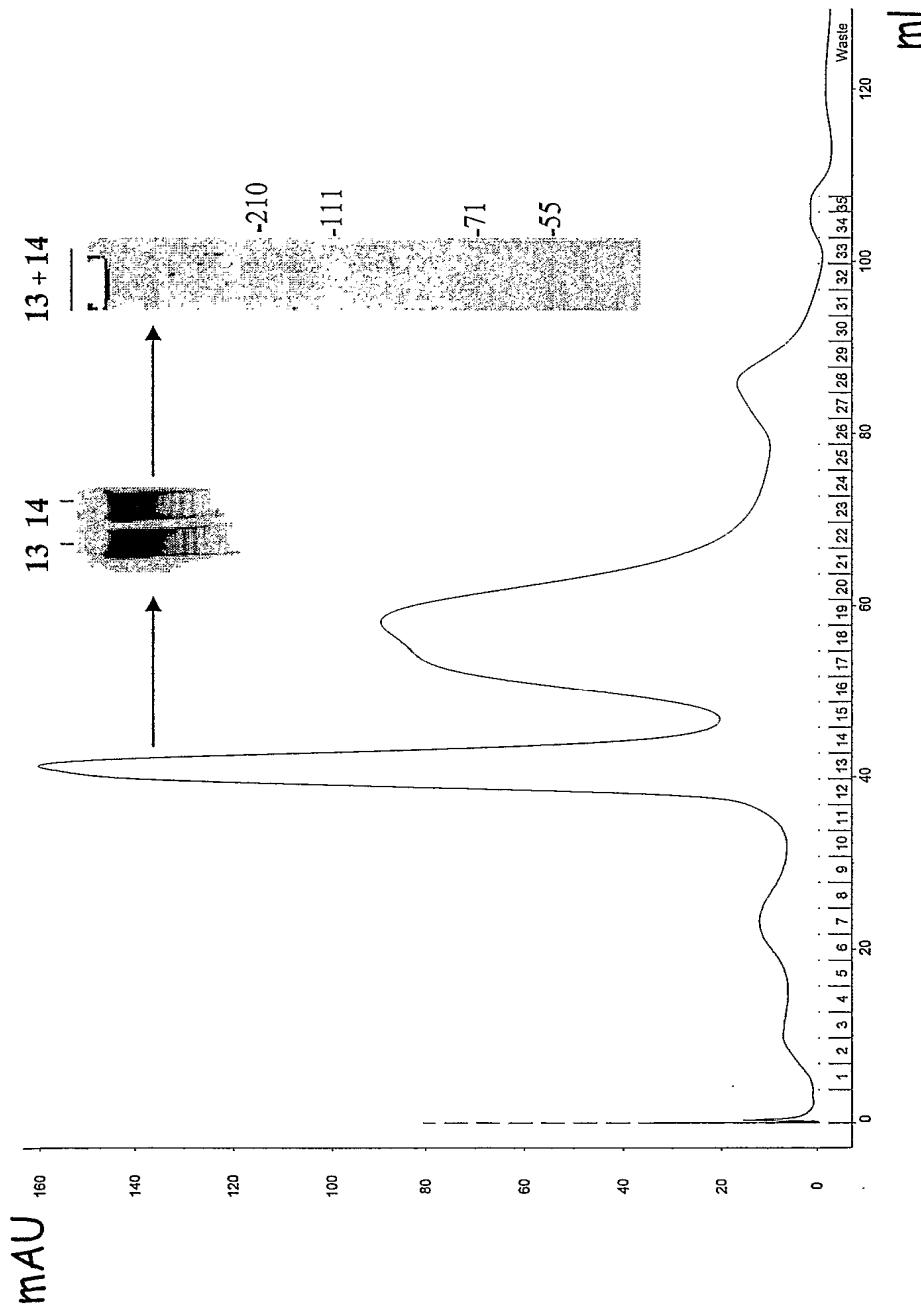
 $\Delta\text{Mean} < 100$  $\alpha\text{-}104$  $\Delta\text{Mean} < 298$  $\Delta\text{Mean} < 100$  $\Delta\text{Mean} < 251$  $\Delta\text{Mean} < 355$  $\Delta\text{Mean} 461$

Figure 170

Phase contrast Microscopy Immuno-electronmicroscopy(Immunogold Negative Staining,
1° α -80, 2° α -mouse gold particles 10nm)*L. lactis**L. lactis + AT-1*

PCT/US05/27239 369/487

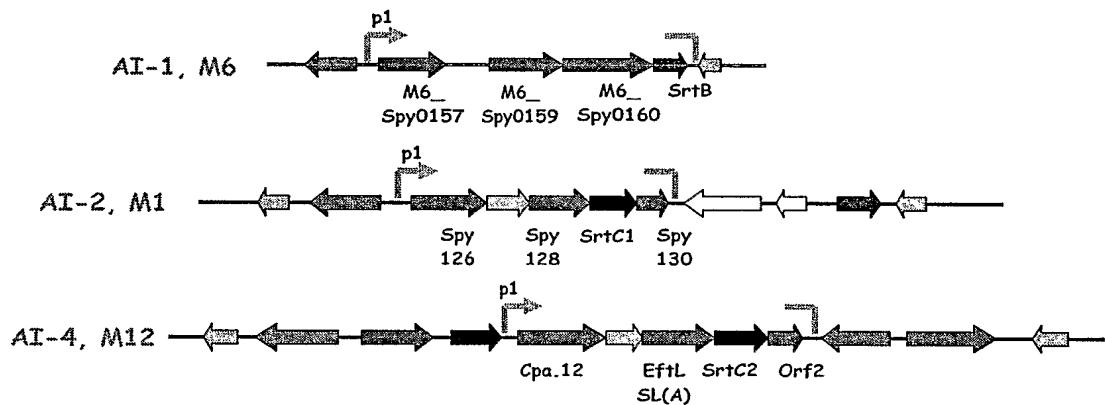
Figure 171

Gel filtration on Sepharyl HR 400

PCT/US05/27239

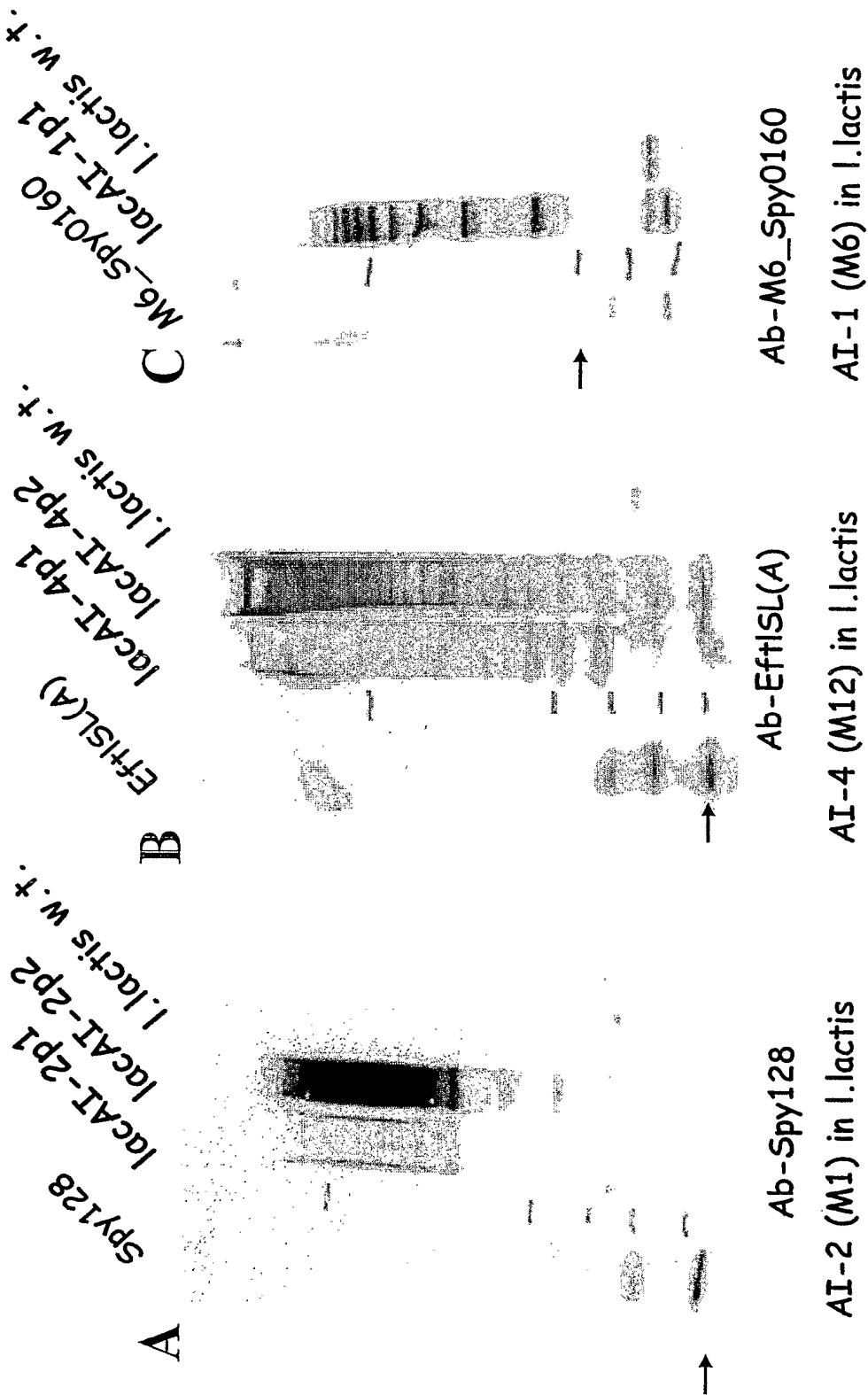
370/487

Figure 172



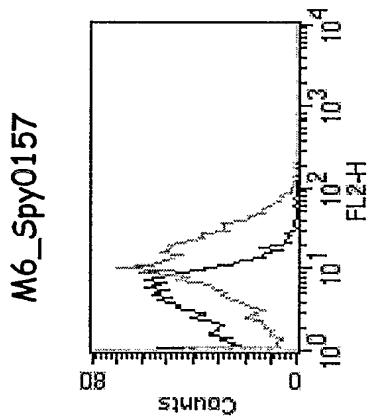
PCT/US05/27239 371/487

Figure 173



372/487

Figure 174



PCT/US05/27239

373/487

Figure 175

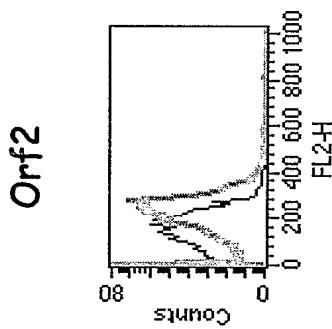
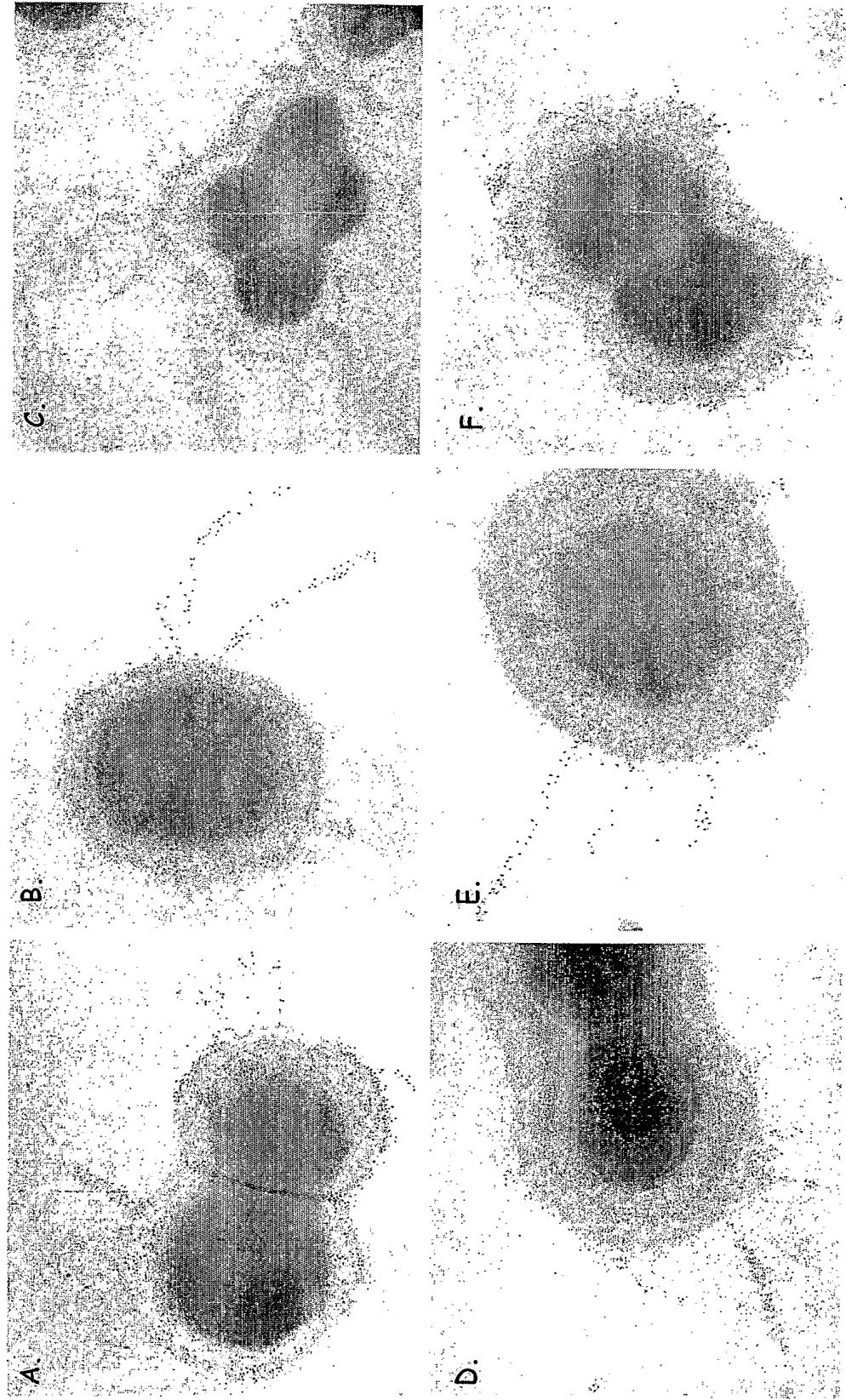


Figure 176



Immuno-gold labeling with antibodies against: A. B. C. D. E. M6_Spy0160; F. M6_Spy0159

Figure 177

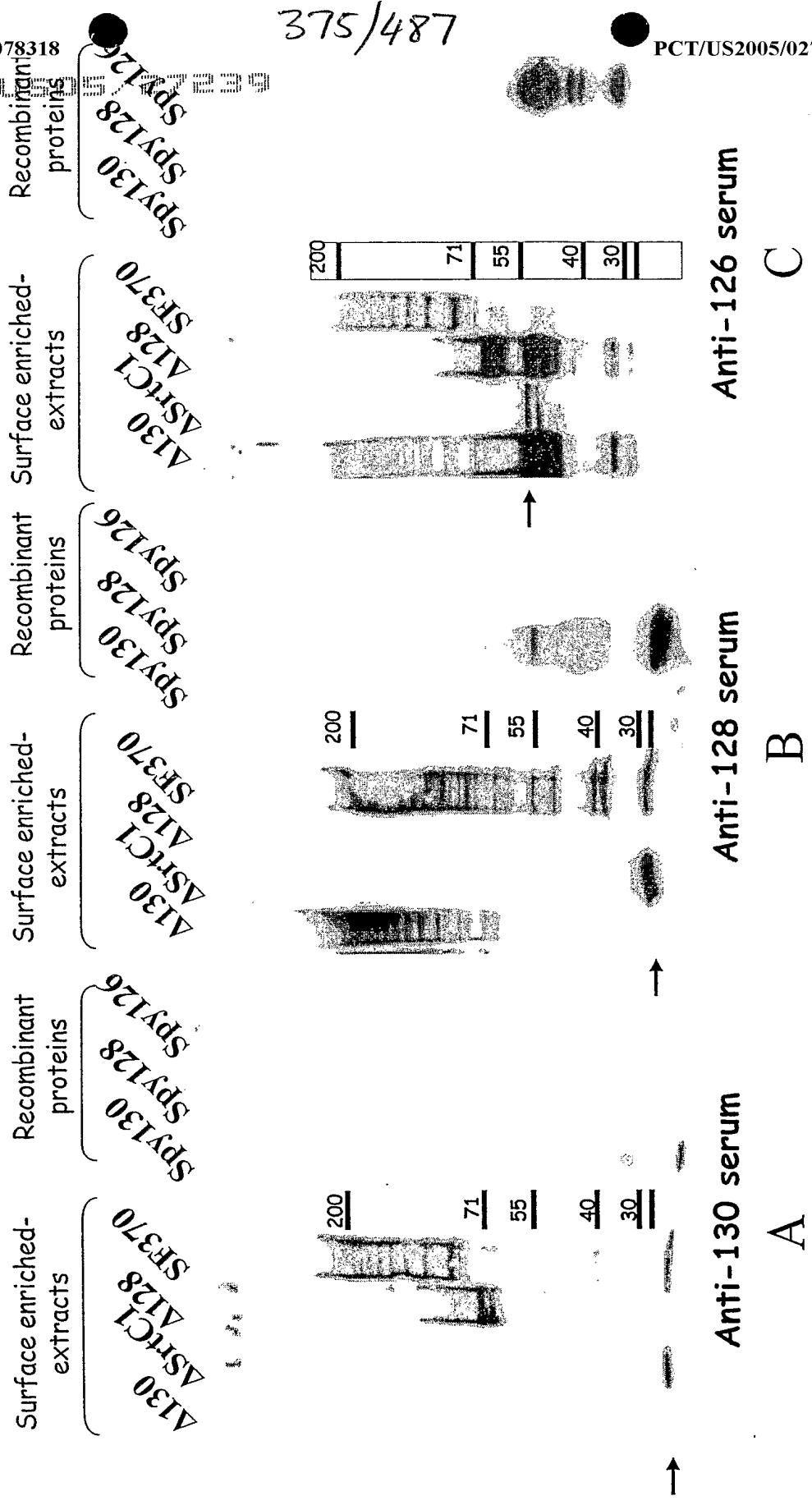
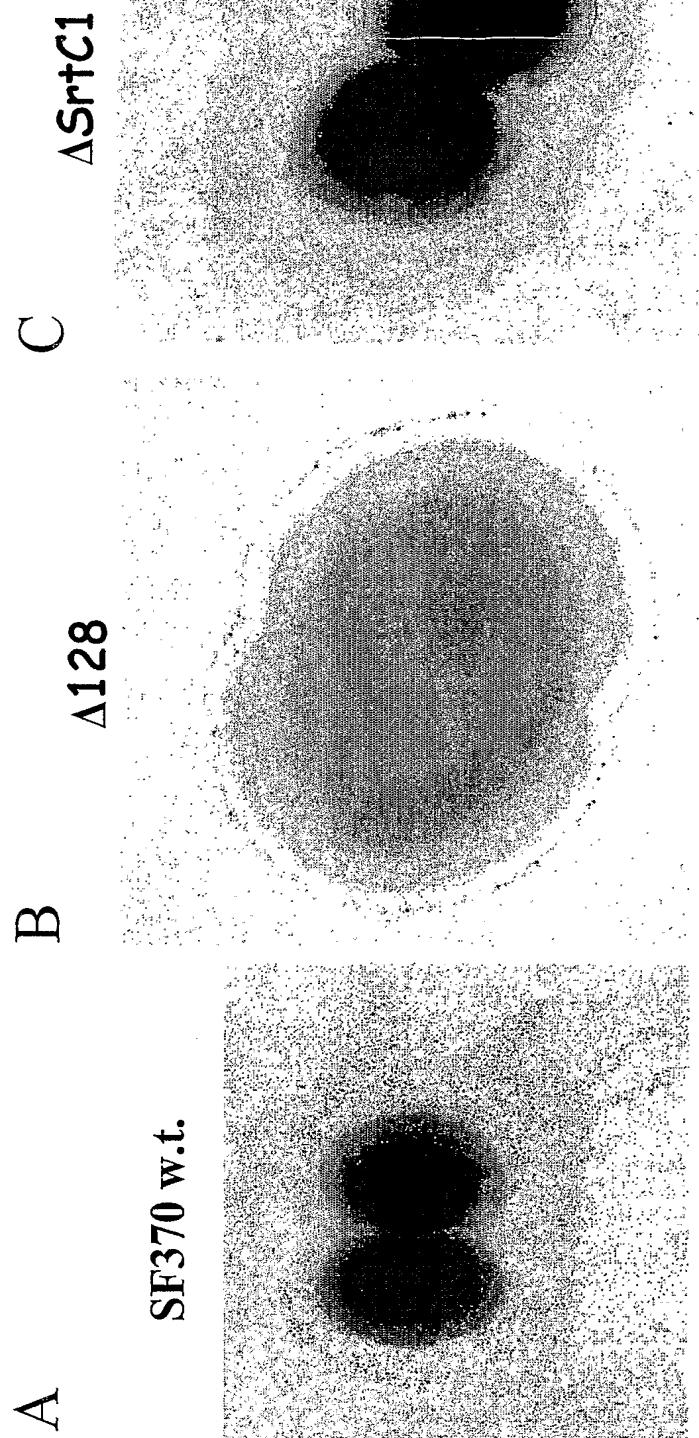


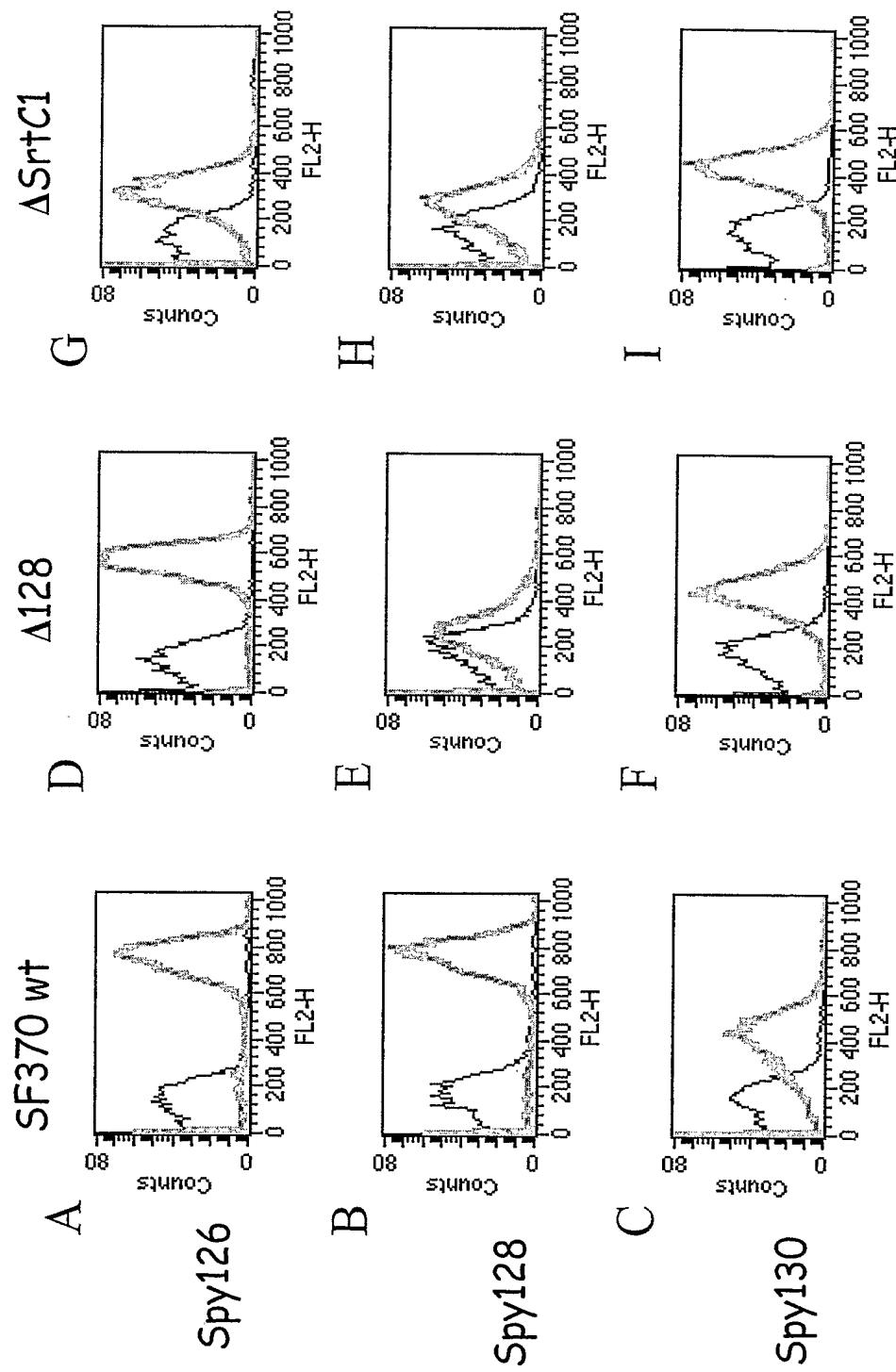
Figure 178



Immuno-gold labeling with sera against Spy128

Comparison of wild type and mutant strain by Immunolectron Microscopy show that Spy128- or SrtC1-lacking bacteria are not able to assemble pili. SrtC1, therefore, is absolutely required for pilus assembly but not for surface anchoring.

Figure 179



PCT/US05/27239 378/487

Figure 180

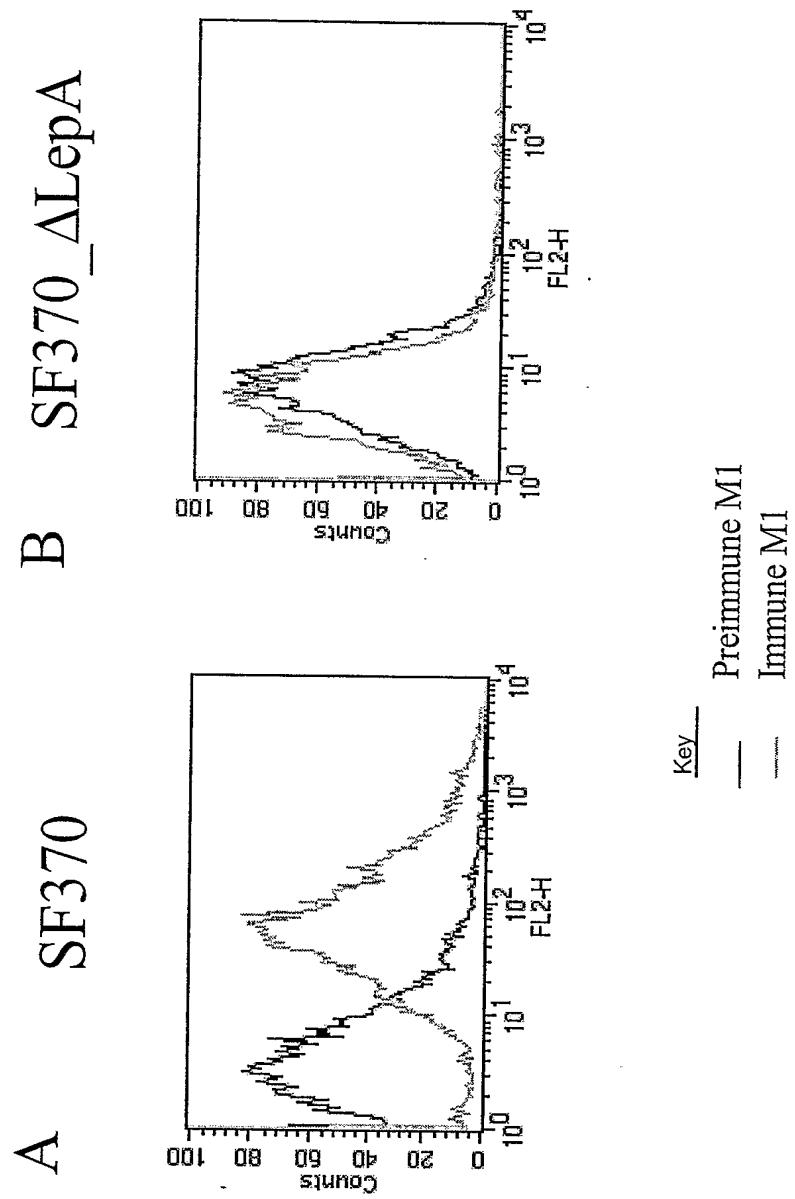


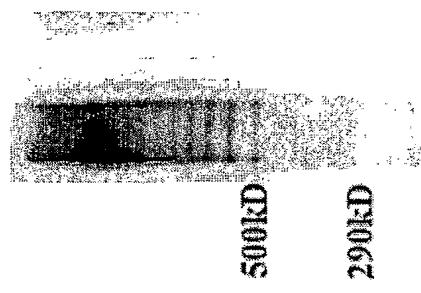
Figure 181

WO 2006/078318
PCT/US05/27239 379/487

PCT/US2005/027239

Pili form high molecular weight
polymers in gradient SDS-PAGE gels

T4A(*wrgA-si*)
T4



α -RrgB

- 1.TIGR4
2. 19A Hungary-6
3. 6B Finland-12
4. 6B II
5. 9V Spain-3
6. 23F Taiwan-15
7. 19F II
8. 1 II
9. D39

Figure 182

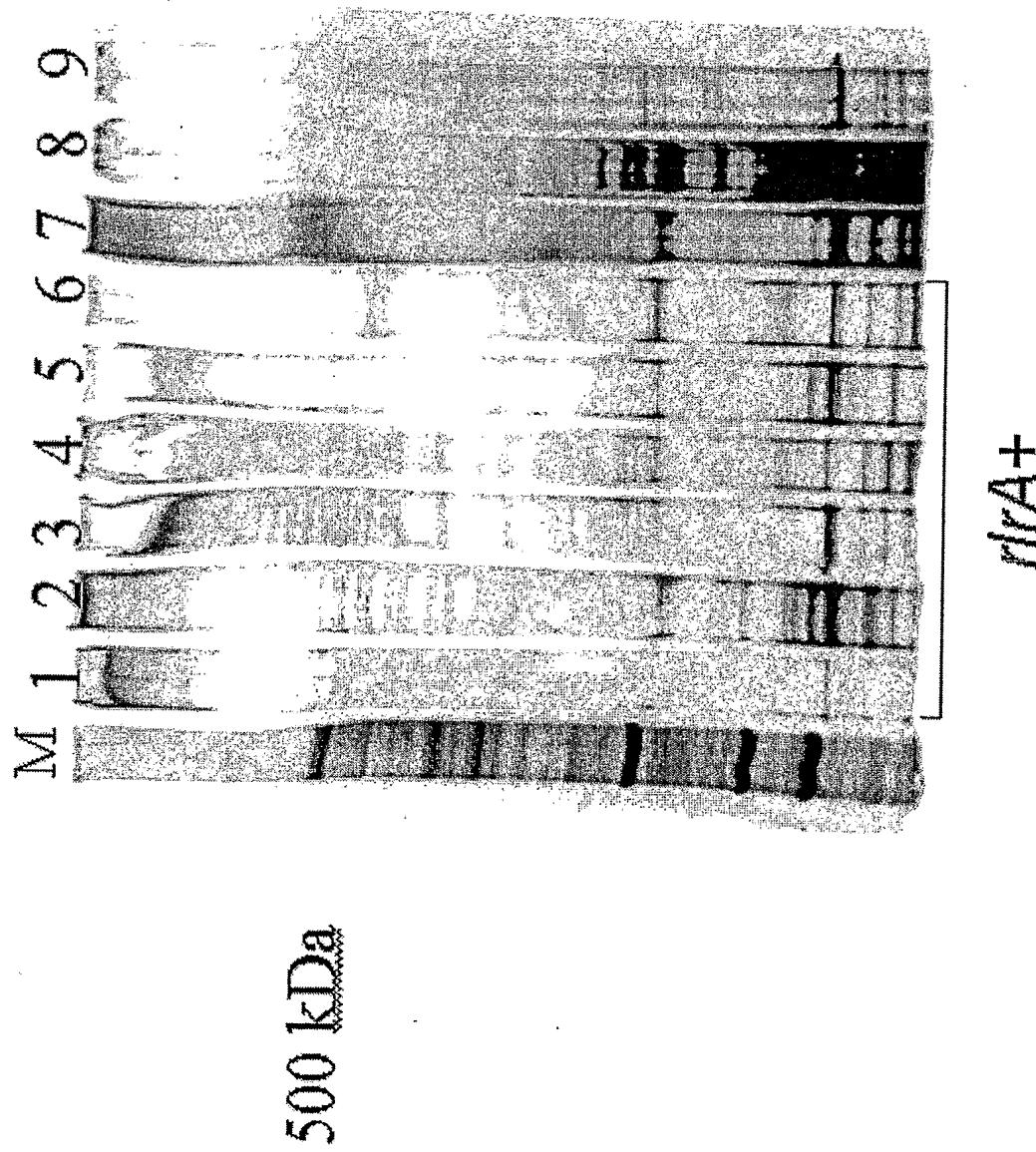


Figure 183

6BFim-12

9VSP3

TIGR4

TIGR4-8A

TIGR4

kDa

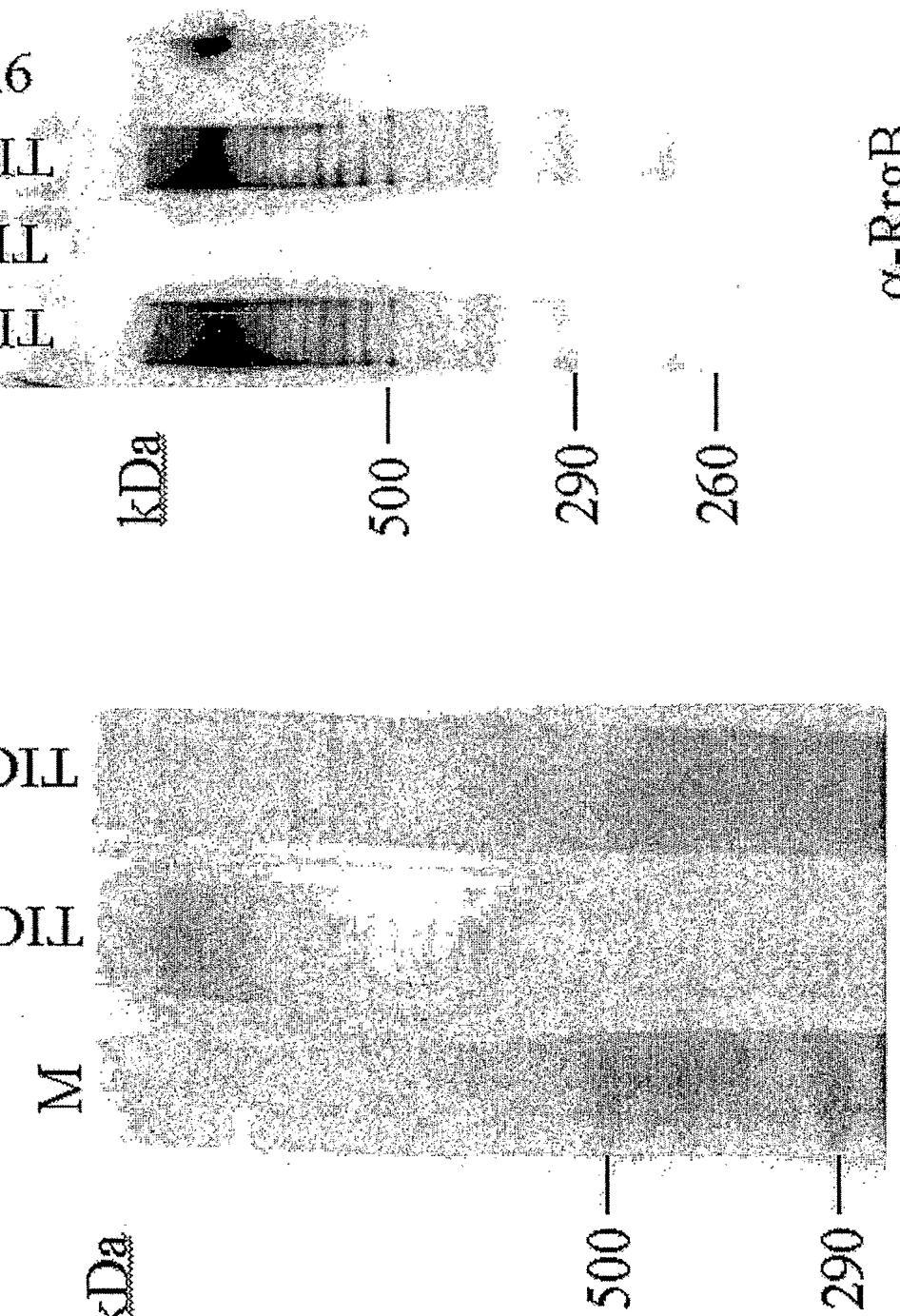
—
500—
290—
260

TIGR4-8A

TIGR4

M

kDa



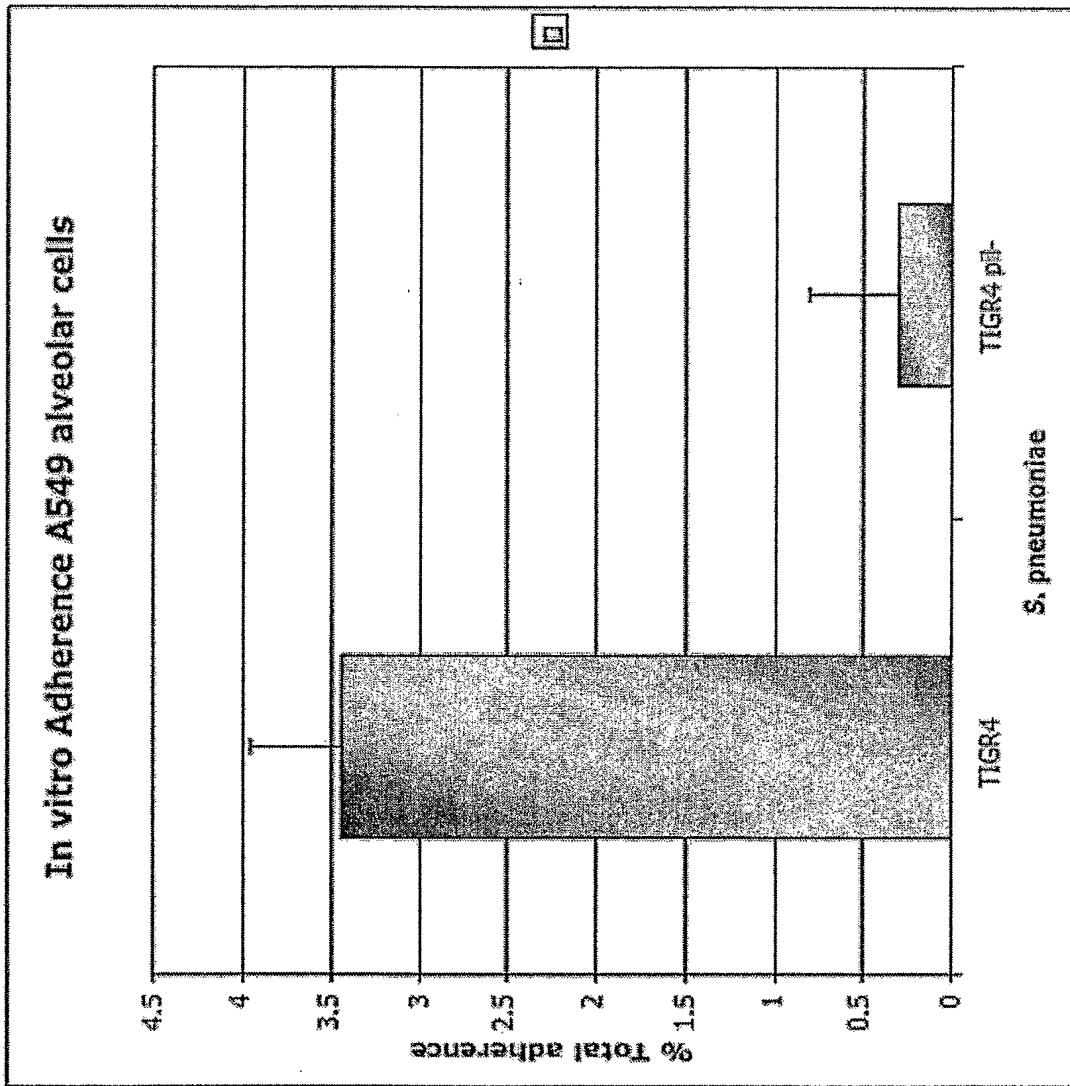
Silver stained gel 3-8%

Anti-RrgB TIGR4 recognized the 9v pili

PCT/US05/27239

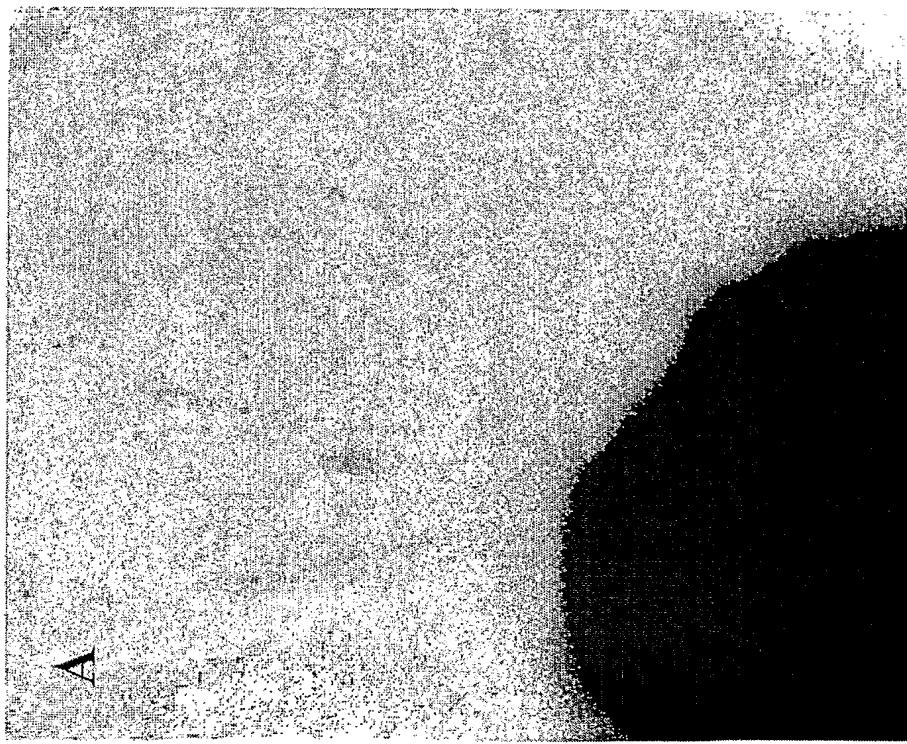
382/487

Figure 184



PCT/US05/27239 383/487

Figure 185



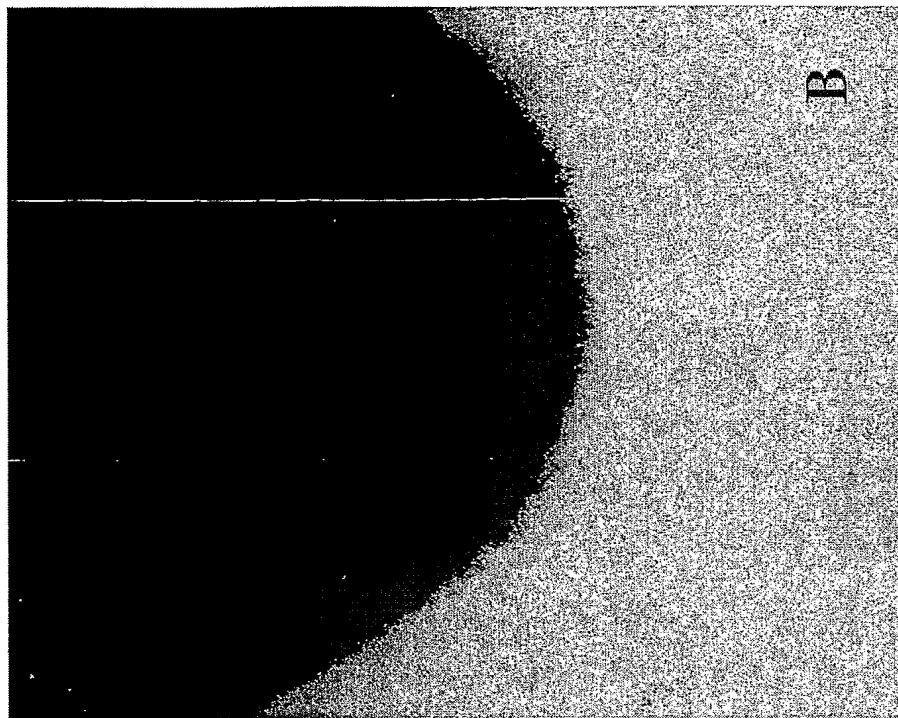


Figure 186

WO 2006/078318

385/487

PCT/US2005/027239

PCT/US05/27239

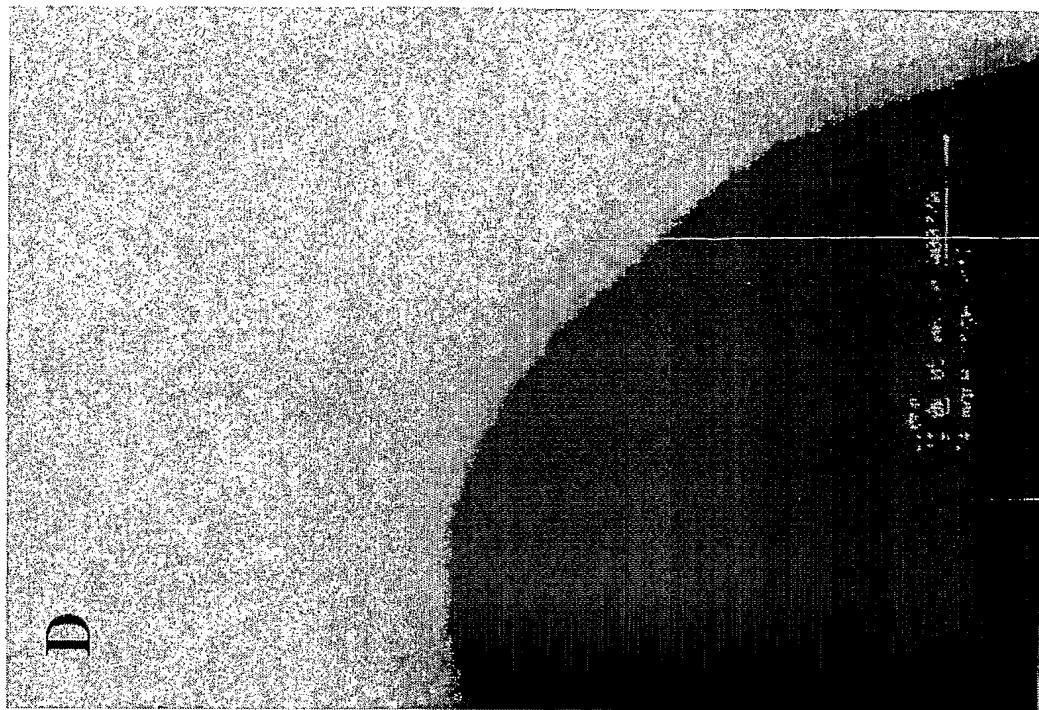


Figure 188

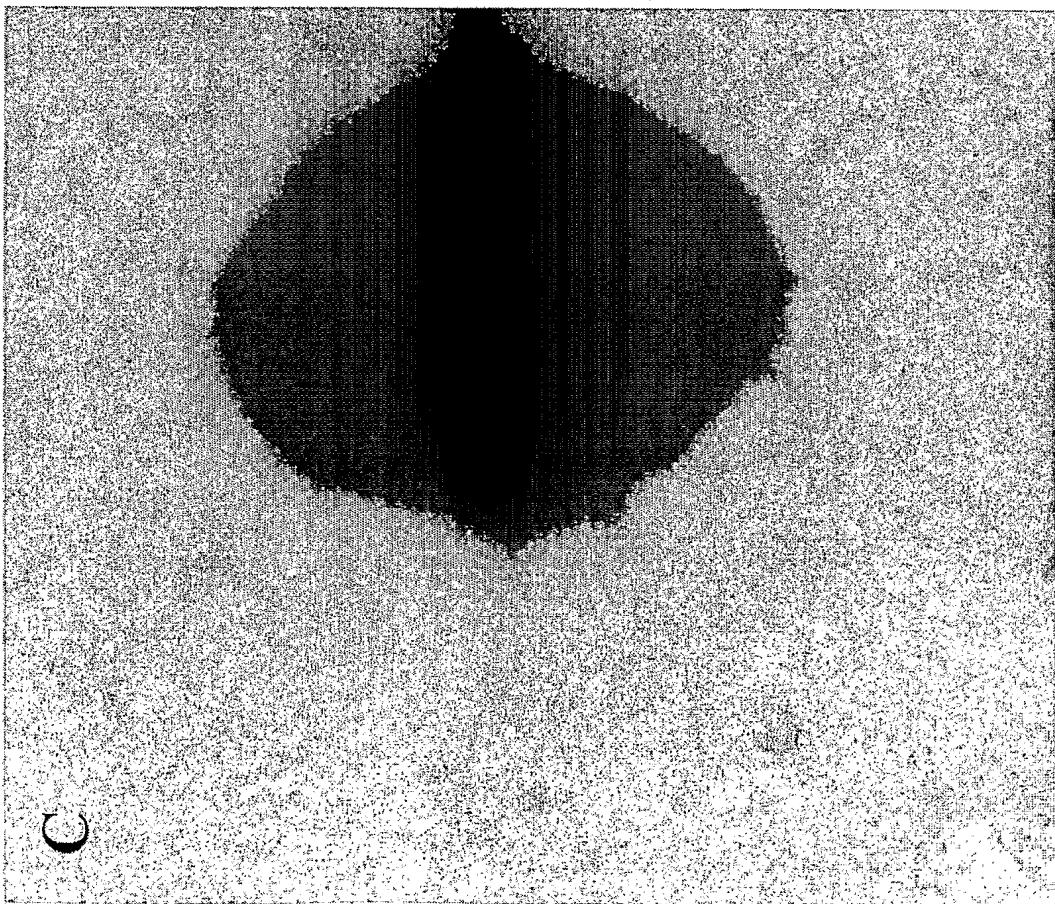


Figure 187

Figure 189

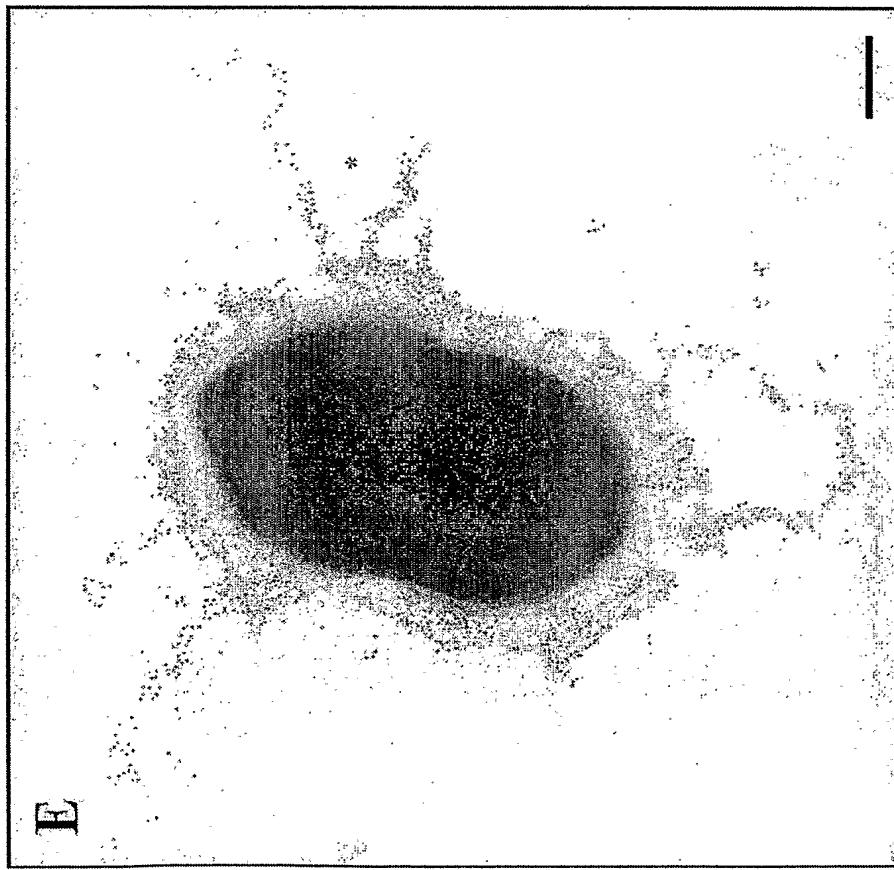


Figure 190

S. pneumoniae pili proteins: sp0462 (Rrg.A)Expression and purification:

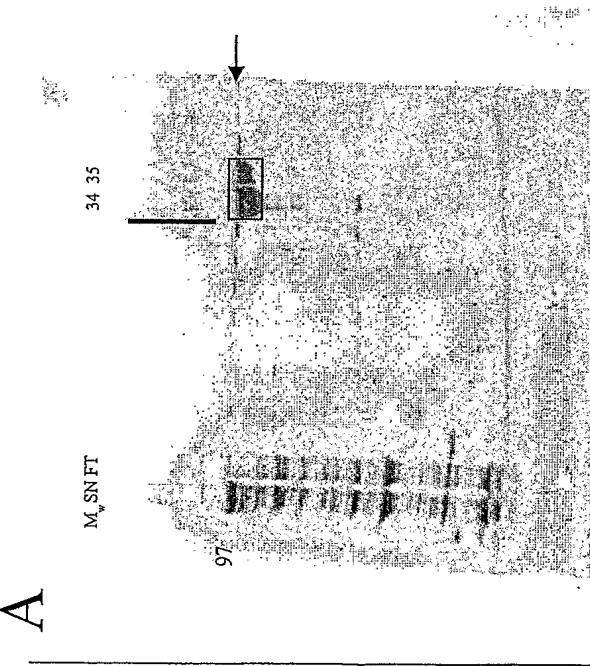
- pET 21b+*-rrgA-6*
- purified in soluble form (stored at -80°C; in NaCl physiol.)



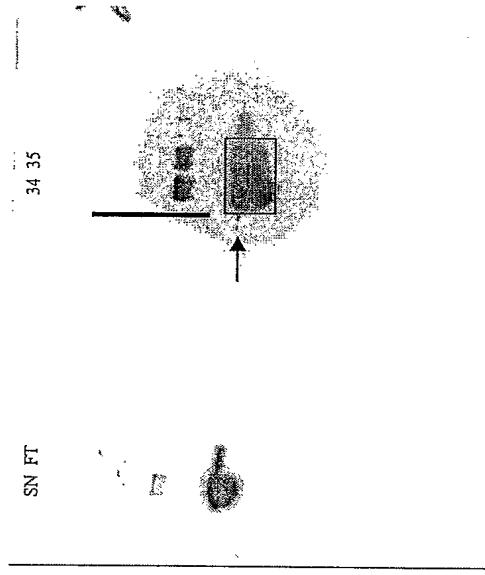
Results:

- protein conc.: 1,1 mg/ml

A



B



SDS-page

Western blot (anti-HIS)

388/487

S. pneumoniae pili proteins – antibody production (mice)

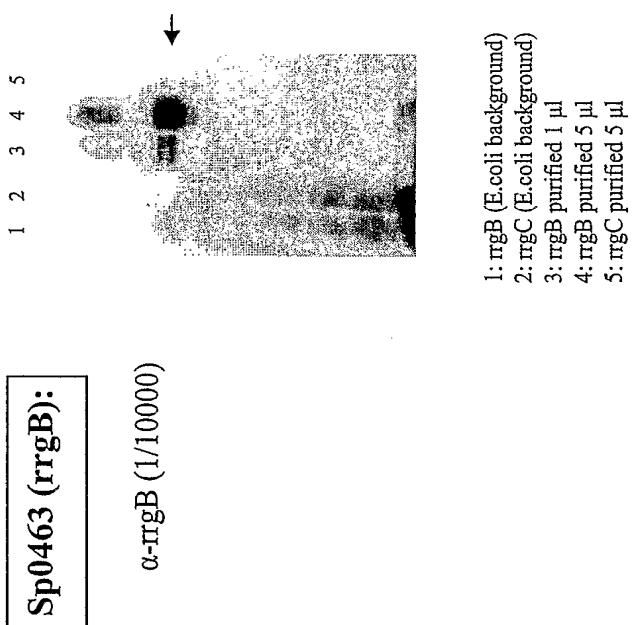


Figure 191

S. pneumoniae pili proteins – antibody production (mice)

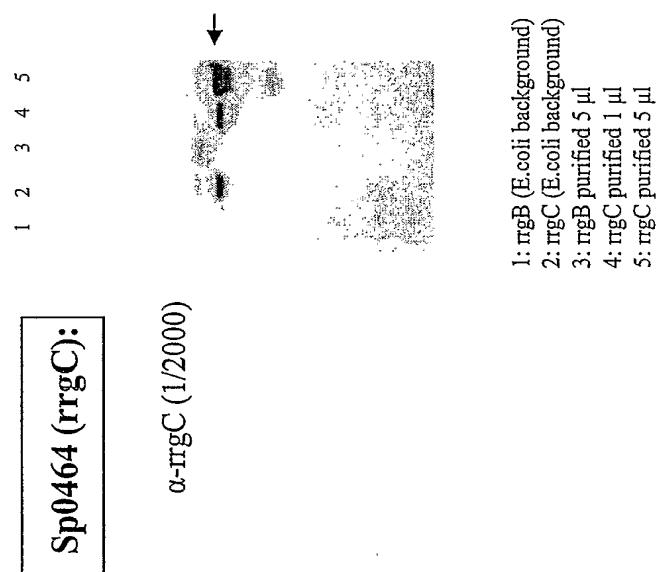


Figure 192

S. pneumoniae TIGR4 pilus purification I – cultivation + digestion

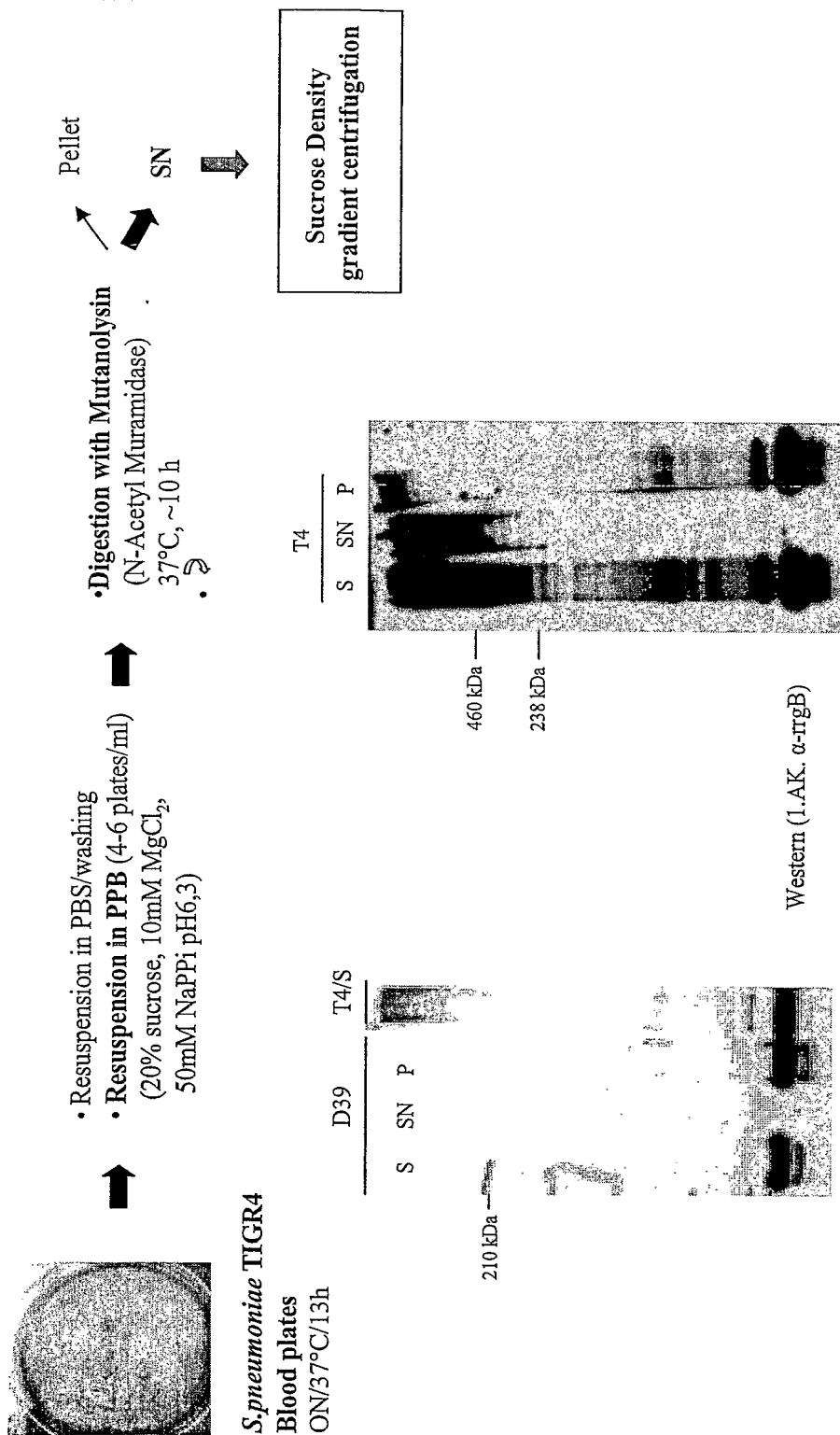


Figure 193

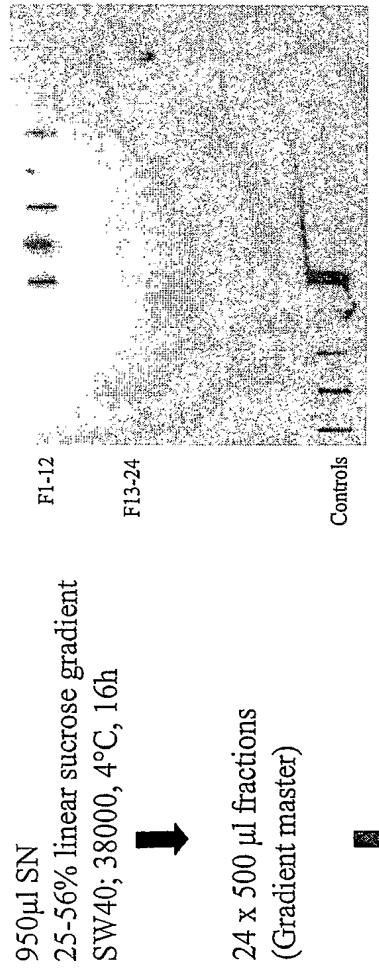
S. pneumoniae TIGR4 pilus purification II - Sucrose density gradient centrifugation

WO 2006/078318

PCT/US05/27239

391/487

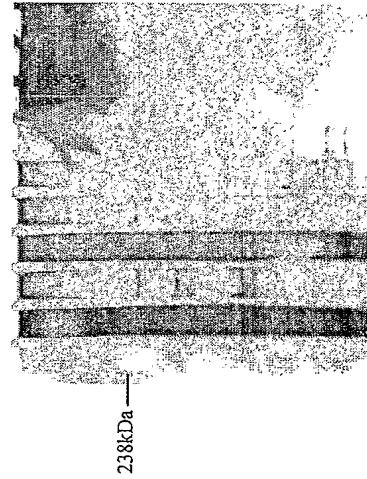
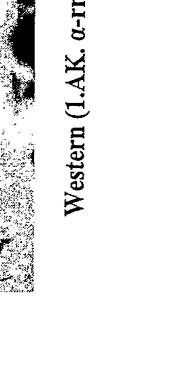
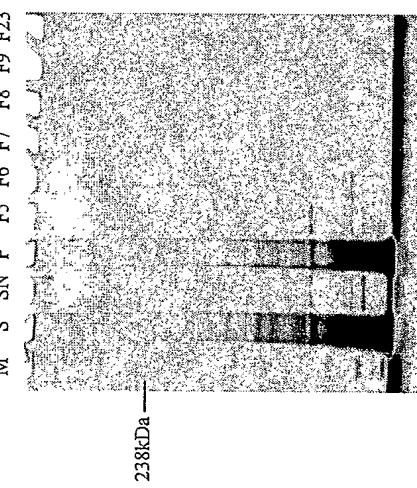
PCT/US2005/027239



Slot blot (fractions sucrose grad.)

Western (1AK. α -rgB)

F3 F4 F5 F6 F7



Coomassie staining

Silver Staining

Figure 194

S. pneumoniae TIGR4 pilus purification III – Gel filtration

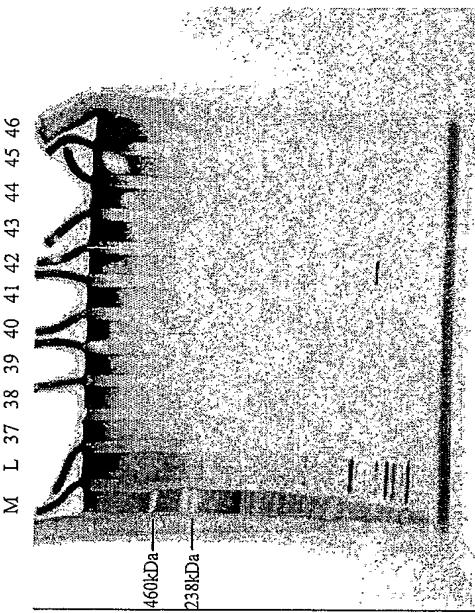
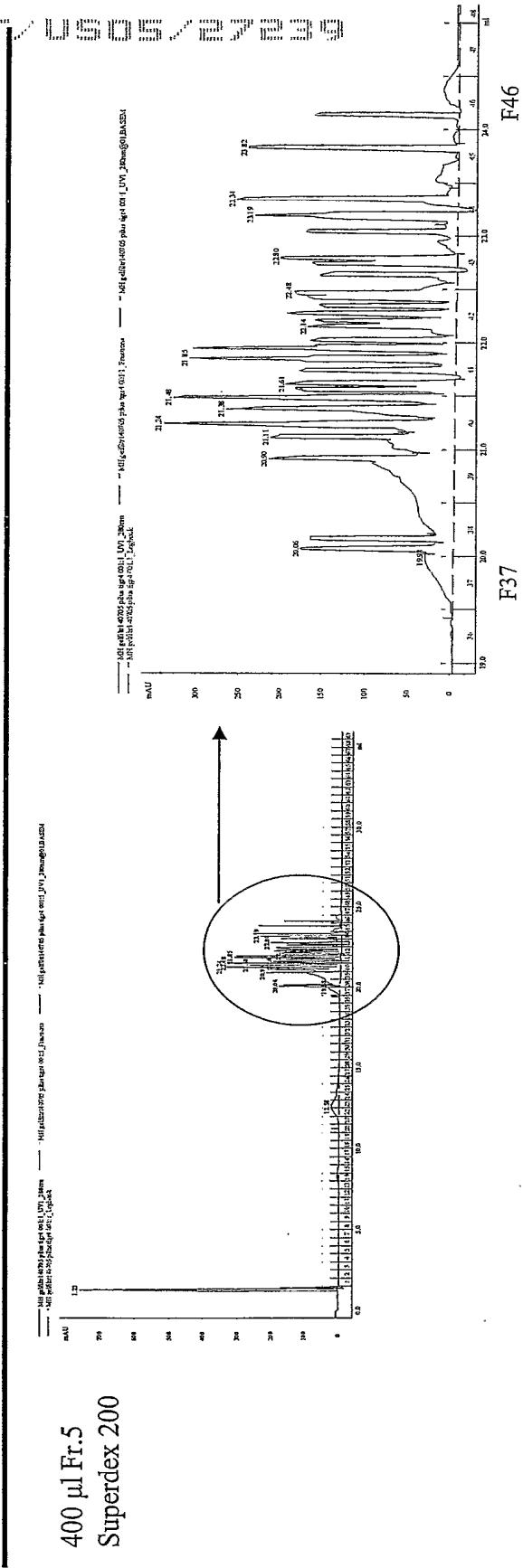


Figure 195

14CSR	-----GTTAGCGCTTTCATTATAAGTCTATGGGACTTTTGATACTCAAAAGC
670	TGAGTTGTTAGCGCTTTCATTATAAGTCTATGGGACTTTTGATACTCAAAAGC
6BF	-----GTTAGCGCTTTCATTATAAGTCTATGGGACTTTTGATACTCAAAAGC
6BSP	-----GCGCTTTCATTATAAGTCTATGGGACTTTTGATACTCAAAAGC
19AH	-----GTTAGCGCTTTCATTATAAGTCTATGGGACTTTTGATACTCAAAAGC
23FPO	-----TTAGCGCTTTCATTATAAGTCTATGGGACTTTTGATACTCAAAAGC
19FTW	-----TTTCATTATAAAATCTTATGGGACTTTTGATACTCAAAAGC
9VSP	-----TTAGCGCTTTCATTATAAGTCTATGGGACTTTTGATACTCAAAAGC
TIGR4	-----TTAGCGCTTTCATTATAAGTCTATGGGACTTTTGATACTCAAAAGC
23FTW	-----GCGCTTTCATTATAAGTCTATGGGACTTTTGATACTCAAAAGC *****
14CSR	CCTATAATCTCCACAGTGGGATTTACCCACTACAGAAATTATAGAGCCAGAAAAAAAC
670	CCTATAATCTCCACAGTGGGATTTACCCACTACAGAAATTATAGAGCCAGAAAAAAAC
6BF	CCTATAATCTCCACAGTGGGATTTACCCACTACAGAAATTATAGAGCCAGAAAAAAAC
6BSP	CCTATAATCTCCACAGTGGGATTTACCCACTACAGAAATTATAGAGCCAGAAAAAAAC
19AH	CCTATAATCTCCACAGTGGGATTTACCCACTACAGAAATTATAGAGCCAGAAAAAAAC
23FPO	CCTATAATCTCCACAGTGGGATTTACCCACTACAGAAATTATAGAGCCAGAAAAAAAC
19FTW	CCTATAATCTCCACAGTGGGATTTACCCACTACAGAAATTATAGAGCCAGAAAAAAAC
9VSP	CCTATAATCTCCACAGTGGGATTTACCCACTACAGAAATTATAGAGCCAGAAAAAAAC
TIGR4	CCTATAATCTCCACAGTGGGATTTACCCACTACAGAAATTATAGAGCCAGAAAAAAAC
23FTW	CCTATAATCTCCACAGTGGGATTTACCCACTACAGAAATTATAGAGCCAGAAAAAAAC *****
14CSR	TTTGTTCACTAGCAGAAACTAGAGAGCAGAAGTGTGTTCTGTTAGATTTACCCAAAC
670	TTTGTTCACTAGCAGAAACTAGAGAGCAGAAGTGTGTTCTGTTAGATTTACCCAAAC
6BF	TTTGTTCACTAGCAGAAACTAGAGAGCAGAAGTGTGTTCTGTTAGATTTACCCAAAC
6BSP	TTTGTTCACTAGCAGAAACTAGAGAGCAGAAGTGTGTTCTGTTAGATTTACCCAAAC
19AH	TTTGTTCACTAGCAGAAACTAGAGAGCAGAAGTGTGTTCTGTTAGATTTACCCAAAC
23FPO	TTTGTTCACTAGCAGAAACTAGAGAGCAGAAGTGTGTTCTGTTAGATTTACCCAAAC
19FTW	TTTGTTCACTAGCAGAAACTAGAGAGCAGAAGTGTGTTCTGTTAGATTTACCCAAAC
9VSP	TTTGTTCACTAGCAGAAACTAGAGAGCAGAAGTGTGTTCTGTTAGATTTACCCAAAC
TIGR4	TTTGTTCACTAGCAGAAACTAGAGAGCAGAAGTGTGTTCTGTTAGATTTACCCAAAC
23FTW	TTTGTTCACTAGCAGAAACTAGAGAGCAGAAGTGTGTTCTGTTAGATTTACCCAAAC *****
14CSR	TGGGAAATATGGGATAAGAATAGAGATGGCTTAGGAAGCCCCCTTTTGTTGAGACAG
670	TGGGAAATATGGGATAAGAATAGAGATGGCTTAGGAAGCCCCCTTTTGTTGAGACAG
6BF	TGGGAAATATGGGATAAGAATAGAGATGGCTTAGGAAGCCCCCTTTTGTTGAGACAG
6BSP	TGGGAAATATGGGATAAGAATAGAGATGGCTTAGGAAGCCCCCTTTTGTTGAGACAG
19AH	TGGGAAATATGGGATAAGAATAGAGATGGCTTAGGAAGCCCCCTTTTGTTGAGACAG
23FPO	TGGGAAATATGGGATAAGAATAGAGATGGCTTAGGAAGCCCCCTTTTGTTGAGACAG
19FTW	TGGGAAATATGGGATAAGAATAGAGATGGCTTAGGAAGCCCCCTTTTGTTGAGACAG
9VSP	TGGGAAATATGGGATAAGAATAGAGATGGCTTAGGAAGCCCCCTTTTGTTGAGACAG
TIGR4	TGGGAAATATGGGATAAGAATAGAGATGGCTTAGGAAGCCCCCTTTTGTTGAGACAG
23FTW	TGGGAAATATGGGATAAGAATAGAGATGGCTTAGGAAGCCCCCTTTTGTTGAGACAG *****
14CSR	TACGATGAACCTATAACAAATAGTGGCCTTTTAGCAATCATTGCGACCCGTTGCAA
670	TACGATGAACCTATAACAAATAGTGGCCTTTTAGCAATCATTGCGACCCGTTGCAA
6BF	TACGATGAACCTATAACAAATAGTGGCCTTTTAGCAATCATTGCGACCCGTTGCAA
6BSP	TACGATGAACCTATAACAAATAGTGGCCTTTTAGCAATCATTGCGACCCGTTGCAA
19AH	TACGATGAACCTATAACAAATAGTGGCCTTTTAGCAATCATTGCGACCCGTTGCAA
23FPO	TACGATGAACCTATAACAAATAGTGGCCTTTTAGCAATCATTGCGACCCGTTGCAA
19FTW	TACGATGAACCTATAACAAATAGTGGCCTTTTAGCAATCATTGCGACCCGTTGCAA
9VSP	TACGATGAACCTATAACAAATAGTGGCCTTTTAGCAATCATTGCGACCCGTTGCAA
TIGR4	TACGATGAACCTATAACAAATAGTGGCCTTTTAGCAATCATTGCGACCCGTTGCAA
23FTW	TACGATGAACCTATAACAAATAGTGGCCTTTTAGCAATCATTGCGACCCGTTGCAA *****

Figure 196A

PCT/US05/27239

14CSR	AAGCCTCTTTCCGGATATCTACAATTGTCGATAGATGAGACGCTGTTGGCTAACATGCA
670	AAGCCTCTTTCCGGATATCTACAATTGTCGATAGATGAGACGCTGTTGGCTAACATGCA
6BF	AAGCCTCTTTCCGGATATCTACAATTGTCGATAGATGAGACGCTGTTGGCTAACATGCA
6BSP	AAGCCTCTTTCCGGATATCTACAATTGTCGATAGATGAGACGCTGTTGGCTAACATGCA
19AH	AAGCCTCTTTCCGGATATCTACAATTGTCGATAGATGAGACGCTGTTGGCTAACATGCA
23FPO	AAGCCTCTTTCCGGATATCTACAATTGTCGATAGATGAGACGCTGTTGGCTAACATGCA
19FTW	AAGCCTCTTTCCGGATATCTACAATTGTCGATAGATGAGACGCTGTTGGCTAACATGCA
9VSP	AAGCCTCTTTCCGGATATCTACAATTGTCGATAGATGAGACGCTGTTGGCTAACATGCA
TIGR4	AAGCCTCTTTCCGGATATCTACAATTGTCGATAGATGAGACGCTGTTGGCTAACATGCA
23FTW	AAGCCTCTTTCCGGATATCTACAATTGTCGATAGATGAGACGCTGTTGGCTAACATGCA

14CSR	AATCTAAGGCAATCGTAAAAAGTGATGTTCCCTTGGGATACTGCTTTAACGTAAG
670	AATCTAAGGCAATCGTAAAAAGTGATGTTCCCTTGGGATACTGCTTTAACGTAAG
6BF	AATCTAAGGCAATCGTAAAAAGTGATGTTCCCTTGGGATACTGCTTTAACGTAAG
6BSP	AATCTAAGGCAATCGTAAAAAGTGATGTTCCCTTGGGATACTGCTTTAACGTAAG
19AH	AATCTAAGGCAATCGTAAAAAGTGATGTTCCCTTGGGATACTGCTTTAACGTAAG
23FPO	AATCTAAGGCAATCGTAAAAAGTGATGTTCCCTTGGGATACTGCTTTAACGTAAG
19FTW	AATCTAAGGCAATCGTAAAAAGTGATGTTCCCTTGGGATACTGCTTTAACGTAAG
9VSP	AATCTAAGGCAATCGTAAAAAGTGATGTTCCCTTGGGATACTGCTTTAACGTAAG
TIGR4	AATCTAAGGCAATCGTAAAAAGTGATGTTCCCTTGGGATACTGCTTTAACGTAAG
23FTW	AATCTAAGGCAATCGTAAAAAGTGATGTTCCCTTGGGATACTGCTTTAACGTAAG

14CSR	GCAGGTATTCTTCGTTGAATAATAATCAATGGCTCTGTCAAATGCTCTCTGAAGGAG
670	GCAGGTATTCTTCGTTGAATAATAATCAATGGCTCTGTCAAATGCTCTCTGAAGGAG
6BF	GCAGGTATTCTTCGTTGAATAATAATCAATGGCTCTGTCAAATGCTCTCTGAAGGAG
6BSP	GCAGGTATTCTTCGTTGAATAATAATCAATGGCTCTGTCAAATGCTCTCTGAAGGAG
19AH	GCAGGTATTCTTCGTTGAATAATAATCAATGGCTCTGTCAAATGCTCTCTGAAGGAG
23FPO	GCAGGTATTCTTCGTTGAATAATAATCAATGGCTCTGTCAAATGCTCTCTGAAGGAG
19FTW	GCAGGTATTCTTCGTTGAATAATAATCAATGGCTCTGTCAAATGCTCTCTGAAGGAG
9VSP	GCAGGTATTCTTCGTTGAATAATAATCAATGGCTCTGTCAAATGCTCTCTGAAGGAG
TIGR4	GCAGGTATTCTTCGTTGAATAATAATCAATGGCTCTGTCAAATGCTCTCTGAAGGAG
23FTW	GCAGGTATTCTTCGTTGAATAATAATCAATGGCTCTGTCAAATGCTCTCTGAAGGAG

14CSR	GAGGACTAATTAGAATATTGTATCCTGAAACAGAGGCAACTTGTCACTAAAATTCCGTA
670	GAGGACTAATTAGAATATTGTATCCTGAAACAGAGGCAACTTGTCACTAAAATTCCGTA
6BF	GAGGACTAATTAGAATATTGTATCCTGAAACAGAGGCAACTTGTCACTAAAATTCCGTA
6BSP	GAGGACTAATTAGAATATTGTATCCTGAAACAGAGGCAACTTGTCACTAAAATTCCGTA
19AH	GAGGACTAATTAGAATATTGTATCCTGAAACAGAGGCAACTTGTCACTAAAATTCCGTA
23FPO	GAGGACTAATTAGAATATTGTATCCTGAAACAGAGGCAACTTGTCACTAAAATTCCGTA
19FTW	GAGGACTAATTAGAATATTGTATCCTGAAACAGAGGCAACTTGTCACTAAAATTCCGTA
9VSP	GAGGACTAATTAGAATATTGTATCCTGAAACAGAGGCAACTTGTCACTAAAATTCCGTA
TIGR4	GAGGACTAATTAGAATATTGTATCCTGAAACAGAGGCAACTTGTCACTAAAATTCCGTA
23FTW	GAGGACTAATTAGAATATTGTATCCTGAAACAGAGGCAACTTGTCACTAAAATTCCGTA

14CSR	AAATAATGGACTTTATTAAGTTACATCTGCTTGATTATTTAAATGATAAAAATCGGGA
670	AAATAATGGACTTTATTAAGTTACATCTGCTTGATTATTTAAATGATAAAAATCGGGA
6BF	AAATAATGGACTTTATTAAGTTACATCTGCTTGATTATTTAAATGATAAAAATCGGGA
6BSP	AAATAATGGACTTTATTAAGTTACATCTGCTTGATTATTTAAATGATAAAAATCGGGA
19AH	AAATAATGGACTTTATTAAGTTACATCTGCTTGATTATTTAAATGATAAAAATCGGGA
23FPO	AAATAATGGACTTTATTAAGTTACATCTGCTTGATTATTTAAATGATAAAAATCGGGA
19FTW	AAATAATGGACTTTATTAAGTTACATCTGCTTGATTATTTAAATGATAAAAATCGGGA
9VSP	AAATAATGGACTTTATTAAGTTACATCTGCTTGATTATTTAAATGATAAAAATCGGGA
TIGR4	AAATAATGGACTTTATTAAGTTACATCTGCTTGATTATTTAAATGATAAAAATCGGGA
23FTW	AAATAATGGACTTTATTAAGTTACATCTGCTTGATTATTTAAATGATAAAAATCGGGA

Figure 196B

Figure 196C

14CSR	TTCCTCTTGTATGCTGAAGAACATCAGTTGAATAGTATGAGTC CTTGATTCCATT
670	TTCCTCTTGTATGCTGAAGAACATCAGTTGAATAGTATGAGTC CTTGATTCCATT
6BF	TTCCTCTTGTATGCTGAAGAACATCAGTTGAATAGTATGAGTC CTTGATTCCATT
6BSP	TTCCTCTTGTATGCTGAAGAACATCAGTTGAATAGTATGAGTC CTTGATTCCATT
19AH	TTCCTCTTGTATGCTGAAGAACATCAGTTGAATAGTATGAGTC CTTGATTCCATT
23FPO	TTCCTCTTGTATGCTGAAGAACATCAGTTGAATAGTATGAGTC CTTGATTCCATT
19FTW	TTCCTCTTGTATGCTGAAGAACATCAGTTGAATAGTATGAGTC CTTGATTCCATT
9VSP	TTCCTCTTGTATGCTGAAGAACATCAGTTGAATAGTATGAGTC CTTGATTCCATT
TIGR4	TTCCTCTTGTATGCTGAAGAACATCAGTTGAATAGTATGAGTC CTTGATTCCATT
23FTW	TTCCTCTTGTATGCTGAAGAACATCAGTTGAATAGTATGAGTC CTTGATTCCATT

14CSR	TGTCTTGGAAAACGAAGAACATTAGCAGAACATAAACC AAAGATATAATCCAGTTCTT
670	TGTCTTGGAAAACGAAGAACATTAGCAGAACATAAACC AAAGATATAATCCAGTTCTT
6BF	TGTCTTGGAAAACGAAGAACATTAGCAGAACATAAACC AAAGATATAATCCAGTTCTT
6BSP	TGTCTTGGAAAACGAAGAACATTAGCAGAACATAAACC AAAGATATAATCCAGTTCTT
19AH	TGTCTTGGAAAACGAAGAACATTAGCAGAACATAAACC AAAGATATAATCCAGTTCTT
23FPO	TGTCTTGGAAAACGAAGAACATTAGCAGAACATAAACC AAAGATATAATCCAGTTCTT
19FTW	TGTCTTGGAAAACGAAGAACATTAGCAGAACATAAACC AAAGATATAATCCAGTTCTT
9VSP	TGTCTTGGAAAACGAAGAACATTAGCAGAACATAAACC AAAGATATAATCCAGTTCTT
TIGR4	TGTCTTGGAAAACGAAGAACATTAGCAGAACATAAACC AAAGATATAATCCAGTTCTT
23FTW	TGTCTTGGAAAACGAAGAACATTAGCAGAACATAAACC AAAGATATAATCCAGTTCTT

14CSR	CCTGAGTAAAGTCATGTTGGCATGTGGCTCTAAGTAAGTTGGCAATGTTCCATCAAA
670	CCTGAGTAAAGTCATGTTGGCATGTGGCTCTAAGTAAGTTGGCAATGTTCCATCAAA
6BF	CCTGAGTAAAGTCATGTTGGCATGTGGCTCTAAGTAAGTTGGCAATGTTCCATCAAA
6BSP	CCTGAGTAAAGTCATGTTGGCATGTGGCTCTAAGTAAGTTGGCAATGTTCCATCAAA
19AH	CCTGAGTAAAGTCATGTTGGCATGTGGCTCTAAGTAAGTTGGCAATGTTCCATCAAA
23FPO	CCTGAGTAAAGTCATGTTGGCATGTGGCTCTAAGTAAGTTGGCAATGTTCCATCAAA
19FTW	CCTGAGTAAAGTCATGTTGGCATGTGGCTCTAAGTAAGTTGGCAATGTTCCATCAAA
9VSP	CCTGAGTAAAGTCATGTTGGCATGTGGCTCTAAGTAAGTTGGCAATGTTCCATCAAA
TIGR4	CCTGAGTAAAGTCATGTTGGCATGTGGCTCTAAGTAAGTTGGCAATGTTCCATCAAA
23FTW	CCTGAGTAAAGTCATGTTGGCATGTGGCTCTAAGTAAGTTGGCAATGTTCCATCAAA

14CSR	TCGGATACATAAAGAGGTTTTAATTTTCAAACCTCTTGGACTCAGGGAACCTCAAGTG
670	TCGGATACATAAAGAGGTTTTAATTTTCAAACCTCTTGGACTCAGGGAACCTCAAGTG
6BF	TCGGATACATAAAGAGGTTTTAATTTTCAAACCTCTTGGACTCAGGGAACCTCAAGTG
6BSP	TCGGATACATAAAGAGGTTTTAATTTTCAAACCTCTTGGACTCAGGGAACCTCAAGTG
19AH	TCGGATACATAAAGAGGTTTTAATTTTCAAACCTCTTGGACTCAGGGAACCTCAAGTG
23FPO	TCGGATACATAAAGAGGTTTTAATTTTCAAACCTCTTGGACTCAGGGAACCTCAAGTG
19FTW	TCGGATACATAAAGAGGTTTTAATTTTCAAACCTCTTGGACTCAGGGAACCTCAAGTG
9VSP	TCGGATACATAAAGAGGTTTTAATTTTCAAACCTCTTGGACTCAGGGAACCTCAAGTG
TIGR4	TCGGATACATAAAGAGGTTTTAATTTTCAAACCTCTTGGACTCAGGGAACCTCAAGTG
23FTW	TCGGATACATAAAGAGGTTTTAATTTTCAAACCTCTTGGACTCAGGGAACCTCAAGTG

14CSR	GAAATTCCCGACGTTCCAAGTGAGTGCCACTAGTATGCTAAAATGAACATACTCGTCAG
670	GAAATTCCCGACGTTCCAAGTGAGTGCCACTAGTATGCTAAAATGAACATACTCGTCAG
6BF	GAAATTCCCGACGTTCCAAGTGAGTGCCACTAGTATGCTAAAATGAACATACTCGTCAG
6BSP	GAAATTCCCGACGTTCCAAGTGAGTGCCACTAGTATGCTAAAATGAACATACTCGTCAG
19AH	GAAATTCCCGACGTTCCAAGTGAGTGCCACTAGTATGCTAAAATGAACATACTCGTCAG
23FPO	GAAATTCCCGACGTTCCAAGTGAGTGCCACTAGTATGCTAAAATGAACATACTCGTCAG
19FTW	GAAATTCCCGACGTTCCAAGTGAGTGCCACTAGTATGCTAAAATGAACATACTCGTCAG
9VSP	GAAATTCCCGACGTTCCAAGTGAGTGCCACTAGTATGCTAAAATGAACATACTCGTCAG
TIGR4	GAAATTCCCGACGTTCCAAGTGAGTGCCACTAGTATGCTAAAATGAACATACTCGTCAG
23FTW	GAAATTCCCGACGTTCCAAGTGAGTGCCACTAGTATGCTAAAATGAACATACTCGTCAG

Figure 196D

PCT/US05/27239 397/487

14CSR	GTGTGATTTCTAACAGTTCATGACTGAGTTGAGAATTAGACTGCACAATCATATGTGTGA
670	GTGTGATTTCTAACAGTTCATGACTGAGTTGAGAATTAGACTGCACAATCATATGTGTGA
6BF	GTGTGATTTCTAACAGTTCATGACTGAGTTGAGAATTAGACTGCACAATCATATGTGTGA
6BSP	GTGTGATTTCTAACAGTTCATGACTGAGTTGAGAATTAGACTGCACAATCATATGTGTGA
19AH	GTGTGATTTCTAACAGTTCATGACTGAGTTGAGAATTAGACTGCACAATCATATGTGTGA
23FPO	GTGTGATTTCTAACAGTTCATGACTGAGTTGAGAATTAGACTGCACAATCATATGTGTGA
19FTW	GTGTGATTTCTAACAGTTCATGACTGAGTTGAGAATTAGACTGCACAATCATATGTGTGA
9VSP	GTGTGATTTCTAACAGTTCATGACTGAGTTGAGAATTAGACTGCACAATCATATGTGTGA
TIGR4	GTGTGATTTCTAACAGTTCATGACTGAGTTGAGAATTAGACTGCACAATCATATGTGTGA
23FTW	GTGTGATTTCTAACAGTTCATGACTGAGTTGAGAATTAGACTGCACAATCATATGTGTGA

14CSR	CCCAATCCATACTTCCATCATTCAAATCATAAATCTCAATACCAAAATGAAACTGGAGGA
670	CCCAATCCATACTTCCATCATTCAAATCATAAATCTCAATACCAAAATGAAACTGGAGGA
6BF	CCCAATCCATACTTCCATCATTCAAATCATAAATCTCAATACCAAAATGAAACTGGAGGA
6BSP	CCCAATCCATACTTCCATCATTCAAATCATAAATCTCAATACCAAAATGAAACTGGAGGA
19AH	CCCAATCCATACTTCCATCATTCAAATCATAAATCTCAATACCAAAATGAAACTGGAGGA
23FPO	CCCAATCCATACTTCCATCATTCAAATCATAAATCTCAATACCAAAATGAAACTGGAGGA
19FTW	CCCAATCCATACTTCCATCATTCAAATCATAAATCTCAATACCAAAATGAAACTGGAGGA
9VSP	CCCAATCCATACTTCCATCATTCAAATCATAAATCTCAATACCAAAATGAAACTGGAGGA
TIGR4	CCCAATCCATACTTCCATCATTCAAATCATAAATCTCAATACCAAAATGAAACTGGAGGA
23FTW	CCCAATCCATACTTCCATCATTCAAATCATAAATCTCAATACCAAAATGAAACTGGAGGA

14CSR	GTGCAATTAAAAAACGAATGCGATTTCAGGACCAACTACTGATTTTACAAGGTCCA
670	GTGCAATTAAAAAACGAATGCGATTTCAGGACCAACTACTGATTTTACAAGGTCCA
6BF	GTGCAATTAAAAAACGAATGCGATTTCAGGACCAACTACTGATTTTACAAGGTCCA
6BSP	GTGCAATTAAAAAACGAATGCGATTTCAGGACCAACTACTGATTTTACAAGGTCCA
19AH	GTGCAATTAAAAAACGAATGCGATTTCAGGACCAACTACTGATTTTACAAGGTCCA
23FPO	GTGCAATTAAAAAACGAATGCGATTTCAGGACCAACTACTGATTTTACAAGGTCCA
19FTW	GTGCAATTAAAAAACGAATGCGATTTCAGGACCAACTACTGATTTTACAAGGTCCA
9VSP	GTGCAATTAAAAAACGAATGCGATTTCAGGACCAACTACTGATTTTACAAGGTCCA
TIGR4	GTGCAATTAAAAAACGAATGCGATTTCAGGACCAACTACTGATTTTACAAGGTCCA
23FTW	GTGCAATTAAAAAACGAATGCGATTTCAGGACCAACTACTGATTTTACAAGGTCCA

14CSR	AACCTACTGAACGTAGTAACAAGCCACACTTTGTCGTACCGGGTAGCCGTGCGATGG
670	AACCTACTGAACGTAGTAACAAGCCACACTTTGTCGTACCGGGTAGCCGTGCGATGG
6BF	AACCTACTGAACGTAGTAACAAGCCACACTTTGTCGTACCGGGTAGCCGTGCGATGG
6BSP	AACCTACTGAACGTAGTAACAAGCCACACTTTGTCGTACCGGGTAGCCGTGCGATGG
19AH	AACCTACTGAACGTAGTAACAAGCCACACTTTGTCGTACCGGGTAGCCGTGCGATGG
23FPO	AACCTACTGAACGTAGTAACAAGCCACACTTTGTCGTACCGGGTAGCCGTGCGATGG
19FTW	AACCTACTGAACGTAGTAACAAGCCACACTTTGTCGTACCGGGTAGCCGTGCGATGG
9VSP	AACCTACTGAACGTAGTAACAAGCCACACTTTGTCGTACCGGGTAGCCGTGCGATGG
TIGR4	AACCTACTGAACGTAGTAACAAGCCACACTTTGTCGTACCGGGTAGCCGTGCGATGG
23FTW	AACCTACTGAACGTAGTAACAAGCCACACTTTGTCGTACCGGGTAGCCGTGCGATGG

14CSR	AAATATACTCTTTTGTAATTGTTAACAGCTTGTAGTACCTTGAGTAAAGAAGC
670	AAATATACTCTTTTGTAATTGTTAACAGCTTGTAGTACCTTGAGTAAAGAAGC
6BF	AAATATACTCTTTTGTAATTGTTAACAGCTTGTAGTACCTTGAGTAAAGAAGC
6BSP	AAATATACTCTTTTGTAATTGTTAACAGCTTGTAGTACCTTGAGTAAAGAAGC
19AH	AAATATACTCTTTTGTAATTGTTAACAGCTTGTAGTACCTTGAGTAAAGAAGC
23FPO	AAATATACTCTTTTGTAATTGTTAACAGCTTGTAGTACCTTGAGTAAAGAAGC
19FTW	AAATATACTCTTTTGTAATTGTTAACAGCTTGTAGTACCTTGAGTAAAGAAGC
9VSP	AAATATACTCTTTTGTAATTGTTAACAGCTTGTAGTACCTTGAGTAAAGAAGC
TIGR4	AAATATACTCTTTTGTAATTGTTAACAGCTTGTAGTACCTTGAGTAAAGAAGC
23FTW	AAATATACTCTTTTGTAATTGTTAACAGCTTGTAGTACCTTGAGTAAAGAAGC

Figure 196E

PCT/US05/272349

398/487

14CSR	GGAGTATTTAAAATAGTGATTGGTTATAAGCTGATGGAAGTAATAATTCTGTTGAT
670	GGAGTATTTAAAATAGTGATTGGTTATAAGCTGATGGAAGTAATAATTCTGTTGAT
6BF	GGAGTATTTAAAATAGTGATTGGTTATAAGCTGATGGAAGTAATAATTCTGTTGAT
6BSP	GGAGTATTTAAAATAGTGATTGGTTATAAGCTGATGGAAGTAATAATTCTGTTGAT
19AH	GGAGTATTTAAAATAGTGATTGGTTATAAGCTGATGGAAGTAATAATTCTGTTGAT
23FPO	GGAGTATTTAAAATAGTGATTGGTTATAAGCTGATGGAAGTAATAATTCTGTTGAT
19FTW	GGAGTATTTAAAATAGTGATTGGTTATAAGCTGATGGAAGTAATAATTCTGTTGAT
9VSP	GGAGTATTTAAAATAGTGATTGGTTATAAGCTGATGGAAGTAATAATTCTGTTGAT
TIGR4	GGAGTATTTAAAATAGTGATTGGTTATAAGCTGATGGAAGTAATAATTCTGTTGAT
23FTW	GGAGTATTTAAAATAGTGATTGGTTATAAGCTGATGGAAGTAATAATTCTGTTGAT

14CSR	GAGAATGGTGGTCGATTAATTGAACTTGTGCGTATCTAAATTAAATGTCAACTCTTCCT
670	GAGAATGGTGGTCGATTAATTGAACTTGTGCGTATCTAAATTAAATGTCAACTCTTCCT
6BF	GAGAATGGTGGTCGATTAATTGAACTTGTGCGTATCTAAATTAAATGTCAACTCTTCCT
6BSP	GAGAATGGTGGTCGATTAATTGAACTTGTGCGTATCTAAATTAAATGTCAACTCTTCCT
19AH	GAGAATGGTGGTCGATTAATTGAACTTGTGCGTATCTAAATTAAATGTCAACTCTTCCT
23FPO	GAGAATGGTGGTCGATTAATTGAACTTGTGCGTATCTAAATTAAATGTCAACTCTTCCT
19FTW	GAGAATGGTGGTCGATTAATTGAACTTGTGCGTATCTAAATTAAATGTCAACTCTTCCT
9VSP	GAGAATGGTGGTCGATTAATTGAACTTGTGCGTATCTAAATTAAATGTCAACTCTTCCT
TIGR4	GAGAATGGTGGTCGATTAATTGAACTTGTGCGTATCTAAATTAAATGTCAACTCTTCCT
23FTW	GAGAATGGTGGTCGATTAATTGAACTTGTGCGTATCTAAATTAAATGTCAACTCTTCCT

14CSR	CGAATGTTCTGTAAATTCCCTGCAAAATGCTTAGGAGACTTTAGATTGTAAATGAAGTTA
670	CGAATGTTCTGTAAATTCCCTGCAAAATGCTTAGGAGACTTTAGATTGTAAATGAAGTTA
6BF	CGAATGTTCTGTAAATTCCCTGCAAAATGCTTAGGAGACTTTAGATTGTAAATGAAGTTA
6BSP	CGAATGTTCTGTAAATTCCCTGCAAAATGCTTAGGAGACTTTAGATTGTAAATGAAGTTA
19AH	CGAATGTTCTGTAAATTCCCTGCAAAATGCTTAGGAGACTTTAGATTGTAAATGAAGTTA
23FPO	CGAATGTTCTGTAAATTCCCTGCAAAATGCTTAGGAGACTTTAGATTGTAAATGAAGTTA
19FTW	CGAATGTTCTGTAAATTCCCTGCAAAATGCTTAGGAGACTTTAGATTGTAAATGAAGTTA
9VSP	CGAATGTTCTGTAAATTCCCTGCAAAATGCTTAGGAGACTTTAGATTGTAAATGAAGTTA
TIGR4	CGAATGTTCTGTAAATTCCCTGCAAAATGCTTAGGAGACTTTAGATTGTAAATGAAGTTA
23FTW	CGAATGTTCTGTAAATTCCCTGCAAAATGCTTAGGAGACTTTAGATTGTAAATGAAGTTA

14CSR AAGTAGACAGTTCATCTAGTCATAGACCGAATATCCAATAATATAATTAAATGGTAA
670 AAGTAGACAGTTCATCTAGTCATAGACCGAATATCCAATAATATAATTAAATGGTAA
6BF AAGTAGACAGTTCATCTAGTCATAGACCGAATATCCAATAATATAATTAAATGGTAA
6BSP AAGTAGACAGTTCATCTAGTCATAGACCGAATATCCAATAATATAATTAAATGGTAA
19AH AAGTAGACAGTTCATCTAGTCATAGACCGAATATCCAATAATATAATTAAATGGTAA
23FPO AAGTAGACAGTTCATCTAGTCATAGACCGAATATCCAATAATATAATTAAATGGTAA
19FTW AAGTAGACAGTTCATCTAGTCATAGACCGAATATCCAATAATATAATTAAATGGTAA
9VSP AAGTAGACAGTTCATCTAGTCATAGACCGAATATCCAATAATATAATTAAATGGTAA
TIGR4 AAGTAGACAGTTCATCTAGTCATAGACCGAATATCCAATAATATAATTAAATGGTAA
23FTW AAGTAGACAGTTCATCTAGTCATAGACCGAATATCCAATAATATAATTAAATGGTAA

Figure 196F

PCT/LIS05/27239 399/487

14CSR	ATATAGATAAATTAAATTATAACAAAAGAAAACAATTGTCTTGTCAAAAAGGTTG
670	ATATAGATAAATTAAATTATAACAAAAGAAAACAATTGTCTTGTCAAAAAGGTTG
6BF	ATATAGATAAATTAAATTATAACAAAAGAAAACAATTGTCTTGTCAAAAAGGTTG
6BSP	ATATAGATAAATTAAATTATAACAAAAGAAAACAATTGTCTTGTCAAAAAGGTTG
19AH	ATATAGATAAATTAAATTATAACAAAAGAAAACAATTGTCTTGTCAAAAAGGTTG
23FPO	ATATAGATAAATTAAATTATAACAAAAGAAAACAATTGTCTTGTCAAAAAGGTTG
19FTW	ATATAGATAAATTAAATTATAACAAAAGAAAACAATTGTCTTGTCAAAAAGGTTG
9VSP	ATATAGATAAATTAAATTATAACAAAAGAAAACAATTGTCTTGTCAAAAAGGTTG
TIGR4	ATATAGATAAATTAAATTATAACAAAAGAAAACAATTGTCTTGTCAAAAAGGTTG
23FTW	ATATAGATAAATTAAATTATAACAAAAGAAAACAATTGTCTTGTCAAAAAGGTTG

14CSR	TGGAATTTCGACTTTATTGATAAAAACAGCATGTAATAAAGGCATTAAAGATAGTAA
670	TGGAATTTCGACTTTATTGATAAAAACAGCATGTAATAAAGGCATTAAAGATAGTAA
6BF	TGGAATTTCGACTTTATTGATAAAAACAGCATGTAATAAAGGCATTAAAGATAGTAA
6BSP	TGGAATTTCGACTTTATTGATAAAAACAGCATGTAATAAAGGCATTAAAGATAGTAA
19AH	TGGAATTTCGACTTTATTGATAAAAACAGCATGTAATAAAGGCATTAAAGATAGTAA
23FPO	TGGAATTTCGACTTTATTGATAAAAACAGCATGTAATAAAGGCATTAAAGATAGTAA
19FTW	TGGAATTTCGACTTTATTGATAAAAACAGCATGTAATAAAGGCATTAAAGATAGTAA
9VSP	TGGAATTTCGACTTTATTGATAAAAACAGCATGTAATAAAGGCATTAAAGATAGTAA
TIGR4	TGGAATTTCGACTTTATTGATAAAAACAGCATGTAATAAAGGCATTAAAGATAGTAA
23FTW	TGGAATTTCGACTTTATTGATAAAAACAGCATGTAATAAAGGCATTAAAGATAGTAA

14CSR	TGAGTATTGGTGGAGTTTATGGCTTATTTTTTATTAGAAAATATTTTTATCAAAT
670	TGAGTATTGGTGGAGTTTATGGCTTATTTTTTATTAGAAAATATTTTTATCAAAT
6BF	TGAGTATTGGTGGAGTTTATGGCTTATTTTTTATTAGAAAATATTTTTATCAAAT
6BSP	TGAGTATTGGTGGAGTTTATGGCTTATTTTTTATTAGAAAATATTTTTATCAAAT
19AH	TGAGTATTGGTGGAGTTTATGGCTTATTTTTTATTAGAAAATATTTTTATCAAAT
23FPO	TGAGTATTGGTGGAGTTTATGGCTTATTTTTTATTAGAAAATATTTTTATCAAAT
19FTW	TGAGTATTGGTGGAGTTTATGGCTTATTTTTTATTAGAAAATATTTTTATCAAAT
9VSP	TGAGTATTGGTGGAGTTTATGGCTTATTTTTTATTAGAAAATATTTTTATCAAAT
TIGR4	TGAGTATTGGTGGAGTTTATGGCTTATTTTTTATTAGAAAATATTTTT-ATCAAAT
23FTW	TGAGTATTGGTGGAGTTTATGGCTTATTTTTTATTAGAAAATATTTTTATCAAAT

14CSR	ATTGTCGTTCTATAAAAATATGTGATAAAAATATCTATTGTGATGGAAGGTTGTTTAA
670	ATTGTCGTTCTATAAAAATATGTGATAAAAATATCTATTGTGATGGAAGGTTGTTTAA
6BF	ATTGTCGTTCTATAAAAATATGTGATAAAAATATCTATTGTGATGGAAGGTTGTTTAA
6BSP	ATTGTCGTTCTATAAAAATATGTGATAAAAATATCTATTGTGATGGAAGGTTGTTTAA
19AH	ATTGTCGTTCTATAAAAATATGTGATAAAAATATCTATTGTGATGGAAGGTTGTTTAA
23FPO	ATTGTCGTTCTATAAAAATATGTGATAAAAATATCTATTGTGATGGAAGGTTGTTTAA
19FTW	ATTGTCGTTCTATAAAAATATGTGATAAAAATATCTATTGTGATGGAAGGTTGTTTAA
9VSP	ATTGTCGTTCTATAAAAATATGTGATAAAAATATCTATTGTGATGGAAGGTTGTTTAA
TIGR4	ATTGTCGTTCTATAAAAATATGTGATAAAAATATCTATTGTGATGGAAGGTTGTTTAA
23FTW	ATTGTCGTTCTATAAAAATATGTGATAAAAATATCTATTGTGATGGAAGGTTGTTTAA

14CSR	TTTATACTAGGATAGTTAATAGTAATACTATACTATACTATATTGTATACAAGTGTTCA
670	TTTATACTAGGATAGTTAATAGTAATACTATACTATACTATATTGTATACAAGTGTTCA
6BF	TTTATACTAGGATAGTTAATAGTAATACTATACTATACTATATTGTATACAAGTGTTCA
6BSP	TTTATACTAGGATAGTTAATAGTAATACTATACTATACTATATTGTATACAAGTGTTCA
19AH	TTTATACTAGGATAGTTAATAGTAATACTATACTATACTATATTGTATACAAGTGTTCA
23FPO	TTTATACTAGGATAGTTAATAGTAATACTATACTATACTATATTGTATACAAGTGTTCA
19FTW	TTTATACTAGGATAGTTAATAGTAATACTATACTATACTATATTGTATACAAGTGTTCA
9VSP	TTTATACTAGGATAGTTAATAGTAATACTATACTATACTATATTGTATACAAGTGTTCA
TIGR4	TTTATACTAGGATAGTTAATAGTAATACTATACTATACTATATTGTATACAAGTGTTCA
23FTW	TTTATACTAGGATAGTTAATAGTAATACTATACTATACTATATTGTATACAAGTGTTCA

Figure 196G

PCT/US05/27239 400/487

14CSR	TTGCCAGGTGAGAAGATAGCTATAACGCACTTTTACGCTTTGCTACGTTGGTAGT
670	TTGCCAGGTGAGAAGATAGCTATAACGCACTTTTACGCTTTGCTACGTTGGTAGT
6BF	TTGCCAGGTGAGAAGATAGCTATAACGCACTTTTACGCTTTGCTACGTTGGTAGT
6BSP	TTGCCAGGTGAGAAGATAGCTATAACGCACTTTTACGCTTTGCTACGTTGGTAGT
19AH	TTGCCAGGTGAGAAGATAGCTATAACGCACTTTTACGCTTTGCTACGTTGGTAGT
23FPO	TTGCCAGGTGAGAAGATAGCTATAACGCACTTTTACGCTTTGCTACGTTGGTAGT
19FTW	TTGCCAGGTGAGAAGATAGCTATAACGCACTTTTACGCTTTGCTACGTTGGTAGT
9VSP	TTGCCAGGTGAGAAGATAGCTATAACGCACTTTTACGCTTTGCTACGTTGGTAGT
TIGR4	TTGCCAGGTGAGAAGATAGCTATAACGCACTTTTACGCTTTGCTACGTTGGTAGT
23FTW	TTGCCAGGTGAGAAGATAGCTATAACGCACTTTTACGCTTTGCTACGTTGGTAGT *****
14CSR	GAACGGATTAACTCAG--TGAGATAAATTTATCAGAACATAAGTAATCCGTTCTCGT
670	GAACGGATTAACTCAG--TGAGATAAATTTATCAGAACATAAGTAATCCGTTCTCGT
6BF	GAACGGATTAACTCAG--TGAGATAAATTTATCAGAACATAAGTAATCCGTTCTCGT
6BSP	GAACGGATTAACTCAG--TGAGATAAATTTATCAGAACATAAGTAATCCGTTCTCGT
19AH	GAACGGATTAACTCAGCATGAGATAAATTTATCAGAA--TAAGTAATCCGTTCTCGT
23FPO	GAACGGATTAACTCAGCATGAGATAAATTTATCAGAA--TAAGTAATCCGTTCTCGT
19FTW	GAACGGATTAACTCAG--TGAGATAAATTTATCAGAACATAAGTAATCCGTTCTCGT
9VSP	GAACGGATTAACTCAG--TGAGATAAATTTATCAGAACATAAGTAATCCGTTCTCGT
TIGR4	GAACGGATTAACTCAG--TGAGATAAATTTATCAGAACATAAGTAATCCGTTCTCGT
23FTW	GAACGGATTAACTCAG--TGAGATAAATTTATCAGAACATAAGTAATCCGTTCTCGT *****
14CSR	GTATACAGATTGAAAAGTACCTATGAATCATAGAAGGATTAACCTGTTCTATGAATAATGC
670	GTATACAGATTGAAAAGTACCTATGAATCATAGAAGGATTAACCTGTTCTATGAATAATGC
6BF	GTATACAGATTGAAAAGTACCTATGAATCATAGAAGGATTAACCTGTTCTATGAATAATGC
6BSP	GTATACAGATTGAAAAGTACCTATGAATCATAGAAGGATTAACCTGTTCTATGAATAATGC
19AH	GTATACAGATTGAAAAGTACCTATGAATCATAGAAGGATTAACCTGTTCTATGAATAATGC
23FPO	GTATACAGATTGAAAAGTACCTATGAATCATAGAAGGATTAACCTGTTCTATGAATAATGC
19FTW	GTATACAGATTGAAAAGTACCTATGAATCATAGAAGGATTAACCTGTTCTATGAATAATGC
9VSP	GTATACAGATTGAAAAGTACCTATGAATCATAGAAGGATTAACCTGTTCTATGAATAATGC
TIGR4	GTATACAGATTGAAAAGTACCTATGAATCATAGAAGGATTAACCTGTTCTATGAATAATGC
23FTW	GTATACAGATTGAAAAGTACCTATGAATCATAGAAGGATTAACCTGTTCTATGAATAATGC *****
14CSR	TTAACAGGGAGACACACATGAAAAAAAGTAAGAAGATATTCAGAAGGCAGTTGCAGGAC
670	TTAACAGGGAGACACACATGAAAAAAAGTAAGAAGATATTCAGAAGGCAGTTGCAGGAC
6BF	TTAACAGGGAGACACACATGAAAAAAAGTAAGAAGATATTCAGAAGGCAGTTGCAGGAC
6BSP	TTAACAGGGAGACACACATGAAAAAAAGTAAGAAGATATTCAGAAGGCAGTTGCAGGAC
19AH	TTAACAGGGAGACACACATGAAAAAAAGTAAGAAGATATTCAGAAGGCAGTTGCAGGAC
23FPO	TTAACAGGGAGACACACATGAAAAAAAGTAAGAAGATATTCAGAAGGCAGTTGCAGGAC
19FTW	TTAACAGGGAGACACACATGAAAAAAAGTAAGAAGATATTCAGAAGGCAGTTGCAGGAC
9VSP	TTAACAGGGAGACACACATGAAAAAAAGTAAGAAGATATTCAGAAGGCAGTTGCAGGAC
TIGR4	TTAACAGGGAGACACACATGAAAAAAAGTAAGAAGATATTCAGAAGGCAGTTGCAGGAC
23FTW	TTAACAGGGAGACACACATGAAAAAAAGTAAGAAGATATTCAGAAGGCAGTTGCAGGAC *****
14CSR	TGTGCTGTATATCTCAGTTGACAGCTTTCTCGATAGTTGCTTTAGCAGAAACGCCTG
670	TGTGCTGTATATCTCAGTTGACAGCTTTCTCGATAGTTGCTTTAGCAGAAACGCCTG
6BF	TGTGCTGTATATCTCAGTTGACAGCTTTCTCGATAGTTGCTTTAGCAGAAACGCCTG
6BSP	TGTGCTGTATATCTCAGTTGACAGCTTTCTCGATAGTTGCTTTAGCAGAAACGCCTG
19AH	TGTGCTGTATATCTCAGTTGACAGCTTTCTCGATAGTTGCTTTAGCAGAAACGCCTG
23FPO	TGTGCTGTATATCTCAGTTGACAGCTTTCTCGATAGTTGCTTTAGCAGAAACGCCTG
19FTW	TGTGCTGTATATCTCAGTTGACAGCTTTCTCGATAGTTGCTTTAGCAGAAACGCCTG
9VSP	TGTGCTGTATATCTCAGTTGACAGCTTTCTCGATAGTTGCTTTAGCAGAAACGCCTG
TIGR4	TGTGCTGTATATCTCAGTTGACAGCTTTCTCGATAGTTGCTTTAGCAGAAACGCCTG
23FTW	TGTGCTGTATATCTCAGTTGACAGCTTTCTCGATAGTTGCTTTAGCAGAAACGCCTG *****

Figure 196H

PCT/US05/2239

14CSR AAACCAGTCCAGCGATAGGAAAAGTAGTGATTAAGGGAGACAGGCGAAGGGAGGAGCGCTTC
 670 AAACCAGTCCAGCGATAGGAAAAGTAGTGATTAAGGGAGACAGGCGAAGGGAGGAGCGCTTC
 6BF AAACCAGTCCAGCGATAGGAAAAGTAGTGATTAAGGGAGACAGGCGAAGGGAGGAGCGCTTC
 6BSP AAACCAGTCCAGCGATAGGAAAAGTAGTGATTAAGGGAGACAGGCGAAGGGAGGAGCGCTTC
 19AH AAACCAGTCCAGCGATAGGAAAAGTAGTGATTAAGGGAGACAGGCGAAGGGAGGAGCGCTTC
 23FPO AAACCAGTCCAGCGATAGGAAAAGTAGTGATTAAGGGAGACAGGCGAAGGGAGGAGCGCTTC
 19FTW AAACCAGTCCAGCGATAGGAAAAGTAGTGATTAAGGGAGACAGGCGAAGGGAGGAGCGCTTC
 9VSP AAACCAGTCCAGCGATAGGAAAAGTAGTGATTAAGGGAGACAGGCGAAGGGAGGAGCGCTTC
 TIGR4 AAACCAGTCCAGCGATAGGAAAAGTAGTGATTAAGGGAGACAGGCGAAGGGAGGAGCGCTTC
 23FTW AAACCAGTCCAGCGATAGGAAAAGTAGTGATTAAGGGAGACAGGCGAAGGGAGGAGCGCTTC

14CSR TAGGAGATGCCGTCTTGAGTTGAAAAACAATAACGGATGGCACAACTGTTCGCAAAGGA
 670 TAGGAGATGCCGTCTTGAGTTGAAAAACAATAACGGATGGCACAACTGTTCGCAAAGGA
 6BF TAGGAGATGCCGTCTTGAGTTGAAAAACAATAACGGATGGCACAACTGTTCGCAAAGGA
 6BSP TAGGAGATGCCGTCTTGAGTTGAAAAACAATAACGGATGGCACAACTGTTCGCAAAGGA
 19AH TAGGAGATGCCGTCTTGAGTTGAAAAACAATAACGGATGGCACAACTGTTCGCAAAGGA
 23FPO TAGGAGATGCCGTCTTGAGTTGAAAAACAATAACGGATGGCACAACTGTTCGCAAAGGA
 19FTW TAGGAGATGCCGTCTTGAGTTGAAAAACAATAACGGATGGCACAACTGTTCGCAAAGGA
 9VSP TAGGAGATGCCGTCTTGAGTTGAAAAACAATAACGGATGGCACAACTGTTCGCAAAGGA
 TIGR4 TAGGAGATGCCGTCTTGAGTTGAAAAACAATAACGGATGGCACAACTGTTCGCAAAGGA
 23FTW TAGGAGATGCCGTCTTGAGTTGAAAAACAATAACGGATGGCACAACTGTTCGCAAAGGA

14CSR CAGAGGCCAACAGGAGAACGGATATTTCAACATAAAACCTGGACATACACCTTGA
 670 CAGAGGCCAACAGGAGAACGGATATTTCAACATAAAACCTGGACATACACCTTGA
 6BF CAGAGGCCAACAGGAGAACGGATATTTCAACATAAAACCTGGACATACACCTTGA
 6BSP CAGAGGCCAACAGGAGAACGGATATTTCAACATAAAACCTGGACATACACCTTGA
 19AH CAGAGGCCAACAGGAGAACGGATATTTCAACATAAAACCTGGACATACACCTTGA
 23FPO CAGAGGCCAACAGGAGAACGGATATTTCAACATAAAACCTGGACATACACCTTGA
 19FTW CAGAGGCCAACAGGAGAACGGATATTTCAACATAAAACCTGGACATACACCTTGA
 9VSP CAGAGGCCAACAGGAGAACGGATATTTCAACATAAAACCTGGACATACACCTTGA
 TIGR4 CAGAGGCCAACAGGAGAACGGATATTTCAACATAAAACCTGGACATACACCTTGA
 23FTW CAGAGGCCAACAGGAGAACGGATATTTCAACATAAAACCTGGACATACACCTTGA

14CSR CAGAAGCCAACCTCCAGTTGGTTATAAACCTCTACTAAACAAATGGACTGTTGAAGTTG
 670 CAGAAGCCAACCTCCAGTTGGTTATAAACCTCTACTAAACAAATGGACTGTTGAAGTTG
 6BF CAGAAGCCAACCTCCAGTTGGTTATAAACCTCTACTAAACAAATGGACTGTTGAAGTTG
 6BSP CAGAAGCCAACCTCCAGTTGGTTATAAACCTCTACTAAACAAATGGACTGTTGAAGTTG
 19AH CAGAAGCCAACCTCCAGTTGGTTATAAACCTCTACTAAACAAATGGACTGTTGAAGTTG
 23FPO CAGAAGCCAACCTCCAGTTGGTTATAAACCTCTACTAAACAAATGGACTGTTGAAGTTG
 19FTW CAGAAGCCAACCTCCAGTTGGTTATAAACCTCTACTAAACAAACGGACTGTTGAAGTTG
 9VSP CAGAAGCCAACCTCCAGTTGGTTATAAACCTCTACTAAACAAATGGACTGTTGAAGTTG
 TIGR4 CAGAAGCCAACCTCCAGTTGGTTATAAACCTCTACTAAACAAATGGACTGTTGAAGTTG
 23FTW CAGAAGCCAACCTCCAGTTGGTTATAAACCTCTACTAAACAAATGGACTGTTGAAGTTG

14CSR AGAAGAATGGCGGACACTGTCCAAGGTGAACAGGTAGAAAATCGAGAACAGGGCTCTAT
 670 AGAAGAATGGCGGACACTGTCCAAGGTGAACAGGTAGAAAATCGAGAACAGGGCTCTAT
 6BF AGAAGAATGGCGGACACTGTCCAAGGTGAACAGGTAGAAAATCGAGAACAGGGCTCTAT
 6BSP AGAAGAATGGCGGACACTGTCCAAGGTGAACAGGTAGAAAATCGAGAACAGGGCTCTAT
 19AH AGAAGAATGGCGGACACTGTCCAAGGTGAACAGGTAGAAAATCGAGAACAGGGCTCTAT
 23FPO AGAAGAATGGCGGACACTGTCCAAGGTGAACAGGTAGAAAATCGAGAACAGGGCTCTAT
 19FTW AGAAGAATGGCGGACACTGTCCAAGGTGAACAGGTAGAAAATCGAGAACAGGGCTCTAT
 9VSP AGAAGAATGGCGGACACTGTCCAAGGTGAACAGGTAGAAAATCGAGAACAGGGCTCTAT
 TIGR4 AGAAGAATGGCGGACACTGTCCAAGGTGAACAGGTAGAAAATCGAGAACAGGGCTCTAT
 23FTW AGAAGAATGGCGGACACTGTCCAAGGTGAACAGGTAGAAAATCGAGAACAGGGCTCTAT

PCT/US05/27239

14CSR	CTGACCAGTATCCACAAACAGGGACTTATCCAGATGTTCAAACACCTTATCAGATTATTA
670	CTGACCAGTATCCACAAACAGGGACTTATCCAGATGTTCAAACACCTTATCAGATTATTA
6BF	CTGACCAGTATCCACAAACAGGGACTTATCCAGATGTTCAAACACCTTATCAGATTATTA
6BSP	CTGACCAGTATCCACAAACAGGGACTTATCCAGATGTTCAAACACCTTATCAGATTATTA
19AH	CTGACCAGTATCCACAAACAGGGACTTATCCAGATGTTCAAACACCTTATCAGATTATTA
23FPO	CTGACCAGTATCCACAAACAGGGACTTATCCAGATGTTCAAACACCTTATCAGATTATTA
19FTW	CTGACCAGTATCCACAAACAGGGACTTATCCAGATGTTCAAACACCTTATCAGATTATTA
9VSP	CTGACCAGTATCCACAAACAGGGACTTATCCAGATGTTCAAACACCTTATCAGATTATTA
TIGR4	CTGACCAGTATCCACAAACAGGGACTTATCCAGATGTTCAAACACCTTATCAGATTATTA
23FTW	CTGACCAGTATCCACAAACAGGGACTTATCCAGATGTTCAAACACCTTATCAGATTATTA

14CSR	AGGTAGATGGTCGGAAAAAACGGACAGCACAGCAAGCGTTGAATCCGAATCCATATGAAC
670	AGGTAGATGGTCGGAAAAAACGGACAGCACAGCAAGCGTTGAATCCGAATCCATATGAAC
6BF	AGGTAGATGGTCGGAAAAAACGGACAGCACAGCAAGCGTTGAATCCGAATCCATATGAAC
6BSP	AGGTAGATGGTCGGAAAAAACGGACAGCACAGCAAGCGTTGAATCCGAATCCATATGAAC
19AH	AGGTAGATGGTCGGAAAAAACGGACAGCACAGCAAGCGTTGAATCCGAATCCATATGAAC
23FPO	AGGTAGATGGTCGGAAAAAACGGACAGCACAGCAAGCGTTGAATCCGAATCCATATGAAC
19FTW	AGGTAGATGGTCGGAAAAAACGGACAGCACAGCAAGCGTTGAATCCGAATCCATATGAAC
9VSP	AGGTAGATGGTCGGAAAAAACGGACAGCACAGCAAGCGTTGAATCCGAATCCATATGAAC
TIGR4	AGGTAGATGGTCGGAAAAAACGGACAGCACAGCAAGCGTTGAATCCGAATCCATATGAAC
23FTW	AGGTAGATGGTCGGAAAAAACGGACAGCACAGCAAGCGTTGAATCCGAATCCATATGAAC

14CSR	GTGTGATTCCAGAAGGTACACTTCAAAGAGAATTATCAAGTGAATAATTGGATGATA
670	GTGTGATTCCAGAAGGTACACTTCAAAGAGAATTATCAAGTGAATAATTGGATGATA
6BF	GTGTGATTCCAGAAGGTACACTTCAAAGAGAATTATCAAGTGAATAATTGGATGATA
6BSP	GTGTGATTCCAGAAGGTACACTTCAAAGAGAATTATCAAGTGAATAATTGGATGATA
19AH	GTGTGATTCCAGAAGGTACACTTCAAAGAGAATTATCAAGTGAATAATTGGATGATA
23FPO	GTGTGATTCCAGAAGGTACACTTCAAAGAGAATTATCAAGTGAATAATTGGATGATA
19FTW	GTGTGATTCCAGAAGGTACACTTCAAAGAGAATTATCAAGTGAATAATTGGATGATA
9VSP	GTGTGATTCCAGAAGGTACACTTCAAAGAGAATTATCAAGTGAATAATTGGATGATA
TIGR4	GTGTGATTCCAGAAGGTACACTTCAAAGAGAATTATCAAGTGAATAATTGGATGATA
23FTW	GTGTGATTCCAGAAGGTACACTTCAAAGAGAATTATCAAGTGAATAATTGGATGATA

14CSR	ACCAATATGGAATCGAGTTGACGGTTAGTGGTAAAACGACGGTTGAAACGAAAGGCCT
670	ACCAATATGGAATCGAGTTGACGGTTAGTGGTAAAACGACGGTTGAAACGAAAGGCCT
6BF	ACCAATATGGAATCGAGTTGACGGTTAGTGGTAAAACGACGGTTGAAACGAAAGGCCT
6BSP	ACCAATATGGAATCGAGTTGACGGTTAGTGGTAAAACGACGGTTGAAACGAAAGGCCT
19AH	ACCAATATGGAATCGAGTTGACGGTTAGTGGTAAAACGACGGTTGAAACGAAAGGCCT
23FPO	ACCAATATGGAATCGAGTTGACGGTTAGTGGTAAAACGACGGTTGAAACGAAAGGCCT
19FTW	ACCAATATGGAATCGAGTTGACGGTTAGTGGGAAAACAGTGATGAACGAAAGATAAGT
9VSP	ACCAATATGGAATCGAGTTGACGGTTAGTGGGAAAACAGTGATGAACGAAAGATAAGT
TIGR4	ACCAATATGGAATCGAGTTGACGGTTAGTGGGAAAACAGTGATGAACAAAAGATAAGT
23FTW	ACCAATATGGAATCGAGTTGACGGTTAGTGGGAAAACAGTGATGAACAAAAGATAAGT

14CSR	CTACTCCGCTAGATGTTATTCTATTAGATAACTCCAATAGTATGAGTAATTGAC
670	CTACTCCGCTAGATGTTATTCTATTAGATAACTCCAATAGTATGAGTAATTGAC
6BF	CTACTCCGCTAGATGTTATTCTATTAGATAACTCCAATAGTATGAGTAATTGAC
6BSP	CTACTCCGCTAGATGTTATTCTATTAGATAACTCCAATAGTATGAGTAATTGAC
19AH	CTACTCCGCTAGATGTTATTCTATTAGATAACTCCAATAGTATGAGTAATTGAC
23FPO	CTACTCCGCTAGATGTTATTCTATTAGATAACTCCAATAGTATGAGTAATTGAC
19FTW	CTGTGCCGCTGGATGTCGTTATCTTGCTCGATAACTCAAATAGTATGAGTAACATTGAA
9VSP	CTGTGCCGCTGGATGTCGTTATCTTGCTCGATAACTCAAATAGTATGAGTAACATTGAA
TIGR4	CTGTGCCGCTGGATGTCGTTATCTTGCTCGATAACTCAAATAGTATGAGTAACATTGAA
23FTW	CTGTGCCGCTGGATGTCGTTATCTTGCTCGATAACTCAAATAGTATGAGTAACATTGAA

Figure 196J

PCT/US05/227239

Figure 196K

PCT/US605/27234 404/481

Figure 196L

PCT/LISOS/22723

Figure 196M

Figure 196N

14CSR	AATGATGGTGGCTTGCTAAAAAAATGCAAAAGTGTCTATGATACGACTGAGAAAAGGATT
670	AATGATGGTGGCTTGCTAAAAAAATGCAAAAGTGTCTATGATACGACTGAGAAAAGGATT
6BF	AATGATGGTGGCTTGCTAAAAAAATGCAAAAGTGTCTATGATACGACTGAGAAAAGGATT
6BSP	AATGATGGTGGCTTGCTAAAAAAATGCAAAAGTGTCTATGATACGACTGAGAAAAGGATT
19AH	AATGATGGTGGCTTGCTAAAAAAATGCAAAAGTGTCTATGATACGACTGAGAAAAGGATT
23FPO	AATGATGGTGGCTTGCTAAAAAAATGCAAAAGTGTCTATGATACGACTGAGAAAAGGATT
19FTW	AATGATGGTGGCTTGCTAAAAAAATGCAAAAGTGTCTATGATACGACTGAGAAAAGGATT
9VSP	AATGATGGTGGCTTGCTAAAAAAATGCAAAAGTGTCTATGATACGACTGAGAAAAGGATT
TIGR4	AATGATGGTGGTTTGTAAAAAAATGCAAAAGTGTCTATGATACGACTGAGAAAAGGATT
23FTW	AATGATGGTGGTTTGTAAAAAAATGCAAAAGTGTCTATGATACGACTGAGAAAAGGATT

14CSR	CGTGTAAACAGGTTTGTACCTTGGAACCGGGTAAAAAAGTTACATTGACTTATAATGTTCGC
670	CGTGTAAACAGGTTTGTACCTTGGAACCGGGTAAAAAAGTTACATTGACTTATAATGTTCGC
6BF	CGTGTAAACAGGTTTGTACCTTGGAACCGGGTAAAAAAGTTACATTGACTTATAATGTTCGC
6BSP	CGTGTAAACAGGTTTGTACCTTGGAACCGGGTAAAAAAGTTACATTGACTTATAATGTTCGC
19AH	CGTGTAAACAGGTTTGTACCTTGGAACCGGGTAAAAAAGTTACATTGACTTATAATGTTCGC
23FPO	CGTGTAAACAGGTTTGTACCTTGGAACCGGGTAAAAAAGTTACATTGACTTATAATGTTCGC
19FTW	CGTGTAAACAGGTTTGTACCTTGGAACCGGGTAAAAAAGTTACATTGACTTATAATGTTCGC
9VSP	CGTGTAAACAGGTTTGTACCTTGGAACCGGGTAAAAAAGTTACATTGACTTATAATGTTCGC
TIGR4	CGTGTAAACAGGTTTGTACCTTGGAACCGGGTAAAAAAGTTACATTGACTTACAATGTTCGT
23FTW	CGTGTAAACAGGTTTGTACCTTGGAACCGGGTAAAAAAGTTACATTGACTTACAATGTTCGT

14CSR	TTGAATGACCAATTGTAAAGCAATAAATTCTATGACACGAATGGTCGAACAACCCCTACAC
670	TTGAATGACCAATTGTAAAGCAATAAATTCTATGACACGAATGGTCGAACAACCCCTACAC
6BF	TTGAATGACCAATTGTAAAGCAATAAATTCTATGACACGAATGGTCGAACAACCCCTACAC
6BSP	TTGAATGACCAATTGTAAAGCAATAAATTCTATGACACGAATGGTCGAACAACCCCTACAC
19AH	TTGAATGACCAATTGTAAAGCAATAAATTCTATGACACGAATGGTCGAACAACCCCTACAC
23FPO	TTGAATGACCAATTGTAAAGCAATAAATTCTATGACACGAATGGTCGAACAACCCCTACAC
19FTW	TTGAATGACCAATTGTAAAGCAATAAATTCTATGACACGAATGGTCGAACAACCCCTACAC
9VSP	TTGAATGACCAATTGTAAAGCAATAAATTCTATGACACGAATGGTCGAACAACCCCTACAC
TIGR4	TTGAATGATGAGTTGTAAAGCAATAAATTCTATGACACGAATGGTCGAACAACCCCTACAC
23FTW	TTGAATGATGAGTTGTAAAGCAATAAATTCTATGACACGAATGGTCGAACAACCCCTACAC

14CSR	CCTAAGGAAGTAGAAAAGAACACAGTCGCGGACTTCCC GATT CCTAAGATT CGT GAT GT A
670	CCTAAGGAAGTAGAAAAGAACACAGTCGCGGACTTCCC GATT CCTAAGATT CGT GAT GT A
6BF	CCTAAGGAAGTAGAAAAGAACACAGTCGCGGACTTCCC GATT CCTAAGATT CGT GAT GT A
6BSP	CCTAAGGAAGTAGAAAAGAACACAGTCGCGGACTTCCC GATT CCTAAGATT CGT GAT GT A
19AH	CCTAAGGAAGTAGAAAAGAACACAGTCGCGGACTTCCC GATT CCTAAGATT CGT GAT GT A
23FPO	CCTAAGGAAGTAGAAAAGAACACAGTCGCGGACTTCCC GATT CCTAAGATT CGT GAT GT A
19FTW	CCTAAGGAAGTAGAAAAGAACACAGTCGCGGACTTCCC GATT CCTAAGATT CGT GAT GT A
9VSP	CCTAAGGAAGTAGAAAAGAACACAGTCGCGGACTTCCC GATT CCTAAGATT CGT GAT GT A
TIGR4	CCTAAGGAAGTAGAAAAGAACACAGTCGCGGACTTCCC GATT CCTAAGATT CGT GAT GT A
23FTW	CCTAAGGAAGTAGAAAAGAACACAGTCGCGGACTTCCC GATT CCTAAGATT CGT GAT GT A

14CSR	CGAAAGTATCCAGAAATCACATTCCAAAAGAGAAAAAAACTTGGTGAATTGAGTTTATT
670	CGAAAGTATCCAGAAATCACATTCCAAAAGAGAAAAAAACTTGGTGAATTGAGTTTATT
6BF	CGAAAGTATCCAGAAATCACATTCCAAAAGAGAAAAAAACTTGGTGAATTGAGTTTATT
6BSP	CGAAAGTATCCAGAAATCACATTCCAAAAGAGAAAAAAACTTGGTGAATTGAGTTTATT
19AH	CGAAAGTATCCAGAAATCACATTCCAAAAGAGAAAAAAACTTGGTGAATTGAGTTTATT
23FPO	CGAAAGTATCCAGAAATCACATTCCAAAAGAGAAAAAAACTTGGTGAATTGAGTTTATT
19FTW	CGAAAGTATCCAGAAATCACATTCCAAAAGAGAAAAAAACTTGGTGAATTGAGTTTATT
9VSP	CGAAAGTATCCAGAAATCACATTCCAAAAGAGAAAAAAACTTGGTGAATTGAGTTTATT
TIGR4	CGAAAGTATCCAGAAATCACATTCCAAAAGAGAAAAAAACTTGGTGAATTGAGTTTATT
23FTW	CGAAAGTATCCAGAAATCACATTCCAAAAGAGAAAAAAACTTGGTGAATTGAGTTTATT

Figure 196O

PCT/US05/23329 408/487

14CSR	AAGATCAATAAGAATGATAAAAACACTGAGAGATGCGGTCTTAGTCTCAAAACAA
670	AAGATCAATAAGAATGATAAAAACACTGAGAGATGCGGTCTTAGTCTCAAAACAA
6BF	AAGATCAATAAGAATGATAAAAACACTGAGAGATGCGGTCTTAGTCTCAAAACAA
6BSP	AAGATCAATAAGAATGATAAAAACACTGAGAGATGCGGTCTTAGTCTCAAAACAA
19AH	AAGATCAATAAGAATGATAAAAACACTGAGAGATGCGGTCTTAGTCTCAAAACAA
23FPO	AAGATCAATAAGAATGATAAAAACACTGAGAGATGCGGTCTTAGTCTCAAAACAA
19FTW	AAGATCAATAAGAATGATAAAAACACTGAGAGATGCGGTCTTAGTCTCAAAACAA
9VSP	AAGATCAATAAGAATGATAAAAACACTGAGAGATGCGGTCTTAGTCTCAAAACAA
TIGR4	AAGGTCAATAAAATGATAAAAACACTGAGAGGTGCGGTCTTAGTCTCAAAACAA
23FTW	AAGGTCAATAAAATGATAAAAACACTGAGAGATGCGGTCTTAGTCTCAAAACAA

14CSR	CATCCGGATTATCCAGATATTTATGGAGCTATTGATCAAAATGGCACTTATCAAATGTG
670	CATCCGGATTATCCAGATATTTATGGAGCTATTGATCAAAATGGCACTTATCAAATGTG
6BF	CATCCGGATTATCCAGATATTTATGGAGCTATTGATCAAAATGGCACTTATCAAATGTG
6BSP	CATCCGGATTATCCAGATATTTATGGAGCTATTGATCAAAATGGCACTTATCAAATGTG
19AH	CATCCGGATTATCCAGATATTTATGGAGCTATTGATCAAAATGGCACTTATCAAATGTG
23FPO	CATCCGGATTATCCAGATATTTATGGAGCTATTGATCAAAATGGCACTTATCAAATGTG
19FTW	CATCCGGATTATCCAGATATTTATGGAGCTATTGATCAAAATGGCACTTATCAAATGTG
9VSP	CATCCGGATTATCCAGATATTTATGGAGCTATTGATCAAAATGGCACTTATCAAATGTG
TIGR4	CATCCGGATTATCCAGATATTTATGGAGCTATTGATCAAAATGGCACTTATCAAATGTG
23FTW	CATCCGGATTATCCAGATATTTATGGAGCTATTGATCAAAATGGCACTTATCAAATGTG

14CSR	AGAACAGGTGAAGATGGTAAGTTGACCTTAAAAATCTGTCAGATGGAAATATCGATTA
670	AGAACAGGTGAAGATGGTAAGTTGACCTTAAAAATCTGTCAGATGGAAATATCGATTA
6BF	AGAACAGGTGAAGATGGTAAGTTGACCTTAAAAATCTGTCAGATGGAAATATCGATTA
6BSP	AGAACAGGTGAAGATGGTAAGTTGACCTTAAAAATCTGTCAGATGGAAATATCGATTA
19AH	AGAACAGGTGAAGATGGTAAGTTGACCTTAAAAATCTGTCAGATGGAAATATCGATTA
23FPO	AGAACAGGTGAAGATGGTAAGTTGACCTTAAAAATCTGTCAGATGGAAATATCGATTA
19FTW	AGAACAGGTGAAGATGGTAAGTTGACCTTAAAAATCTGTCAGATGGAAATATCGATTA
9VSP	AGAACAGGTGAAGATGGTAAGTTGACCTTAAAAATCTGTCAGATGGAAATATCGATTA
TIGR4	AGAACAGGTGAAGATGGTAAGTTGACCTTAAAAATCTGTCAGATGGAAATATCGATTA
23FTW	AGAACAGGTGAAGATGGTAAGTTGACCTTAAAAATCTGTCAGATGGAAATATCGATTA

14CSR	TTTGAAAATTCTGAACCAGCTGGTTATAAACCCTCAAAATAAGCCTATCGTTGCCTTC
670	TTTGAAAATTCTGAACCAGCTGGTTATAAACCCTCAAAATAAGCCTATCGTTGCCTTC
6BF	TTTGAAAATTCTGAACCAGCTGGTTATAAACCCTCAAAATAAGCCTATCGTTGCCTTC
6BSP	TTTGAAAATTCTGAACCAGCTGGTTATAAACCCTCAAAATAAGCCTATCGTTGCCTTC
19AH	TTTGAAAATTCTGAACCAGCTGGTTATAAACCCTCAAAATAAGCCTATCGTTGCCTTC
23FPO	TTTGAAAATTCTGAACCAGCTGGTTATAAACCCTCAAAATAAGCCTATCGTTGCCTTC
19FTW	TTTGAAAATTCTGAACCAGCTGGTTATAAACCCTCAAAATAAGCCTATCGTTGCCTTC
9VSP	TTTGAAAATTCTGAACCAGCTGGTTATAAACCCTCAAAATAAGCCTATCGTTGCCTTC
TIGR4	TTTGAAAATTCTGAACCAGCTGGTTATAAACCCTCAAAATAAGCCTATCGTTGCCTTC
23FTW	TTTGAAAATTCTGAACCAGCTGGTTATAAACCCTCAAAATAAGCCTATCGTTGCCTTC

14CSR	CAAATAGTAAATGGAGAAGTCAGAGATGTGACTTCATCGTCCACAAGATATACCAGCG
670	CAAATAGTAAATGGAGAAGTCAGAGATGTGACTTCATCGTCCACAAGATATACCAGCG
6BF	CAAATAGTAAATGGAGAAGTCAGAGATGTGACTTCATCGTCCACAAGATATACCAGCG
6BSP	CAAATAGTAAATGGAGAAGTCAGAGATGTGACTTCATCGTCCACAAGATATACCAGCG
19AH	CAAATAGTAAATGGAGAAGTCAGAGATGTGACTTCATCGTCCACAAGATATACCAGCG
23FPO	CAAATAGTAAATGGAGAAGTCAGAGATGTGACTTCATCGTCCACAAGATATACCAGCG
19FTW	CAAATAGTAAATGGAGAAGTCAGAGATGTGACTTCATCGTCCACAAGATATACCAGCG
9VSP	CAAATAGTAAATGGAGAAGTCAGAGATGTGACTTCATCGTCCACAAGATATACCAGCG
TIGR4	CAAATAGTAAATGGAGAAGTCAGAGATGTGACTTCATCGTCCACAAGATATACCAGCG
23FTW	CAAATAGTAAATGGAGAAGTCAGAGATGTGACTTCATCGTCCACAAGATATACCAGCG

Figure 196P

PCT/US05/233409/487

14CSR	GGTTACGAGTTACGAATGATAAGCACTATATCACAAATGAGCCAATTCTCCAAAAGA
670	GGTTACGAGTTACGAATGATAAGCACTATATCACAAATGAGCCAATTCTCCAAAAGA
6BF	GGTTACGAGTTACGAATGATAAGCACTATATCACAAATGAGCCAATTCTCCAAAAGA
6BSP	GGTTACGAGTTACGAATGATAAGCACTATATCACAAATGAGCCAATTCTCCAAAAGA
19AH	GGTTACGAGTTACGAATGATAAGCACTATATCACAAATGAGCCAATTCTCCAAAAGA
23FPO	GGTTACGAGTTACGAATGATAAGCACTATATCACAAATGAGCCAATTCTCCAAAAGA
19FTW	GGTTACGAGTTACGAATGATAAGCACTATATTACCAATGAACCTATTCTCCAAAGAGA
9VSP	GGTTACGAGTTACGAATGATAAGCACTATATTACCAATGAACCTATTCTCCAAAGAGA
TIGR4	GGTTACGAGTTACGAATGATAAGCACTATATTACCAATGAACCTATTCTCCAAAGAGA
23FTW	GGTTACGAGTTACGAATGATAAGCACTATATTACCAATGAACCTATTCTCCAAAGAGA
	***** * ***** *
14CSR	GAATATCCTCGAACCTGGGTATCGGAATGTTGCCATTCTATCTGATAGGTTGCATGATG
670	GAATATCCTCGAACCTGGGTATCGGAATGTTGCCATTCTATCTGATAGGTTGCATGATG
6BF	GAATATCCTCGAACCTGGGTATCGGAATGTTGCCATTCTATCTGATAGGTTGCATGATG
6BSP	GAATATCCTCGAACCTGGGTATCGGAATGTTGCCATTCTATCTGATAGGTTGCATGATG
19AH	GAATATCCTCGAACCTGGGTATCGGAATGTTGCCATTCTATCTGATAGGTTGCATGATG
23FPO	GAATATCCTCGAACCTGGGTATCGGAATGTTGCCATTCTATCTGATAGGTTGCATGATG
19FTW	GAATATCCTCGAACCTGGGTATCGGAATGTTGCCATTCTATCTGATAGGTTGCATGATG
9VSP	GAATATCCTCGAACCTGGGTATCGGAATGTTGCCATTCTATCTGATAGGTTGCATGATG
TIGR4	GAATATCCTCGAACCTGGGTATCGGAATGTTGCCATTCTATCTGATAGGTTGCATGATG
23FTW	GAATATCCTCGAACCTGGGTATCGGAATGTTGCCATTCTATCTGATAGGTTGCATGATG
	***** * *****
14CSR	ATGGGAGGAGTTCTATTATACACACGGAAACATCCGTAAAGTGTAGCAATGAGAAATGAT
670	ATGGGAGGAGTTCTATTATACACACGGAAACATCCGTAAAGTGTAGCAATGAGAAATGAT
6BF	ATGGGAGGAGTTCTATTATACACACGGAAACATCCGTAAAGTGTAGCAATGAGAAATGAT
6BSP	ATGGGAGGAGTTCTATTATACACACGGAAACATCCGTAAAGTGTAGCAATGAGAAATGAT
19AH	ATGGGAGGAGTTCTATTATACACACGGAAACATCCGTAAAGTGTAGCAATGAGAAATGAT
23FPO	ATGGGAGGAGTTCTATTATACACACGGAAACATCCGTAAAGTGTAGCAATGAGAAATGAT
19FTW	ATGGGAGGAGTTCTATTATACACACGGAAACATCCGTAAAGTGTAG-----AAATGAT
9VSP	ATGGGAGGAGTTCTATTATACACACGGAAACATCCGTAAAGTGTAG-----AAATGAT
TIGR4	ATGGGAGGAGTTCTATTATACACACGGAAACATCCGTAAAGTGTAG-----AAATGAT
23FTW	ATGGGAGGAGTTCTATTATACACACGGAAACATCCGTAAAGTGTAG-----AAATGAT
	***** * *****
14CSR	AATATCGATACTCTGAGCGATACTTTAAGAAGTAGCACTCAAGAAGAGATTAAAGTTA
670	AATATCGATACTCTGAGCGATACTTTAAGAAGTAGCACTCAAGAAGAGATTAAAGTTA
6BF	AATATCGATACTCTGAGCGATACTTTAAGAAGTAGCACTCAAGAAGAGATTAAAGTTA
6BSP	AATATCGATACTCTGAGCGATACTTTAAGAAGTAGCACTCAAGAAGAGATTAAAGTTA
19AH	AATATCGATACTCTGAGCGATACTTTAAGAAGTAGCACTCAAGAAGAGATTAAAGTTA
23FPO	AATATCGATACTCTGAGCGATACTTTAAGAAGTAGCACTCAAGAAGAGATTAAAGTTA
19FTW	AATATCGATACTCTGAGCGATACTTTAAGAAGTAGCACTCAAGAAGAGATTAAAGTTA
9VSP	AATATCGATACTCTGAGCGATACTTTAAGAAGTAGCACTCAAGAAGAGATTAAAGTTA
TIGR4	AATATCGATACTCTGAGCGATACTTTAAGAAGTAGCACTCAAGAAGAGATTAAAGTTA
23FTW	AATATCGATACTCTGAGCGATACTTTAAGAAGTAGCACTCAAGAAGAGATTAAAGTTA
	***** * *****
14CSR	CTTGGTAAAAACAGTTCTTCGCCAAGTAAACCACCATTGAAAGGGGAGATGTTTCGA
670	CTTGGTAAAAACAGTTCTTCGCCAAGTAAACCACCATTGAAAGGGGAGATGTTTCGA
6BF	CTTGGTAAAAACAGTTCTTCGCCAAGTAAACCACCATTGAAAGGGGAGATGTTTCGA
6BSP	CTTGGTAAAAACAGTTCTTCGCCAAGTAAACCACCATTGAAAGGGGAGATGTTTCGA
19AH	CTTGGTAAAAACAGTTCTTCGCCAAGTAAACCACCATTGAAAGGGGAGATGTTTCGA
23FPO	CTTGGTAAAAACAGTTCTTCGCCAAGTAAACCACCATTGAAAGGGGAGATGTTTCGA
19FTW	CTTGGTAAAAACAGTTCTTCGCCAAGTAAACCACCATTGAAAGGGGAGATGTTTCGA
9VSP	CTTGGTAAAAACAGTTCTTCGCCAAGTAAACCACCATTGAAAGGGGAGATGTTTCGA
TIGR4	CTTGGTAAAAACAGTTCTTCGCCAAGTAAACCACCATTGAAAGGGGAGATGTTTCGA
23FTW	CTTGGTAAAAACAGTTCTTCGCCAAGTAAACCACCATTGAAAGGGGAGATGTTTCGA
	***** * *****

Figure 196Q

PCT/US2005/027239 410/487

14CSR	AAACTTGCACAGAAAAAGGATTATTATGTCAATGTGAATTCAATTACATTGCTCACAGT										
670	AAACTTGCACAGAAAAAGGATTATTATGTCAATGTGAATTCAATTACATTGCTCACAGT										
6BF	AAACTTGCACAGAAAAAGGATTATTATGTCAATGTGAATTCAATTACATTGCTCACAGT										
6BSP	AAACTTGCACAGAAAAAGGATTATTATGTCAATGTGAATTCAATTACATTGCTCACAGT										
19AH	AAACTTGCACAGAAAAAGGATTATTATGTCAATGTGAATTCAATTACATTGCTCACAGT										
23FPO	AAACTTGCACAGAAAAAGGATTATTATGTCAATGTGAATTCAATTACATTGCTCACAGT										
19FTW	AAACTTGCACAGAAAAAGGATTATTATGTCAATGTGAATTCAATTACATTGCTCACAGT										
9VSP	AAACTTGCACAGAAAAAGGATTATTATGTCAATGTGAATTCAATTACATTGCTCACAGT										
TIGR4	AAACTTGCACAGAAAAAGGATTATTATGTCAATGTGAATTCAATTACATTGCTCACAGT										
23FTW	AAACTTGCACAGAAAAAGGATTATTATGTCAATGTGAATTCAATTACATTGCTCACAGT										

14CSR	TGATTTAAAGAGATATGAATAAGGGAAATCATGAAATCAATCAACAAATTTTAACAAT										
670	TGATTTAAAGAGATATGAATAAGGGAAATCATGAAATCAATCAACAAATTTTAACAAT										
6BF	TGATTTAAAGAGATATGAATAAGGGAAATCATGAAATCAATCAACAAATTTTAACAAT										
6BSP	TGATTTAAAGAGATATGAATAAGGGAAATCATGAAATCAATCAACAAATTTTAACAAT										
19AH	TGATTTAAAGAGATATGAATAAGGGAAATCATGAAATCAATCAACAAATTTTAACAAT										
23FPO	TGATTTAAAGAGATATGAATAAGGGAAATCATGAAATCAATCAACAAATTTTAACAAT										
19FTW	TGATTTAAAGAGATATGAATAAGGGAAATCATGAAATCAATCAACAAATTTTAACAAT										
9VSP	TGATTTAAAGAGATATGAATAAGGGAAATCATGAAATCAATCAACAAATTTTAACAAT										
TIGR4	TGATTTAAAGAGATATGAATAAGGGAAATCATGAAATCAATCAACAAATTTTAACAAT										
23FTW	TGATTTAAAGAGATATGAATAAGGGAAATCATGAAATCAATCAACAAATTTTAACAAT										

14CSR	GCTTGCTGCCTTATTACTGACAGCGAGTAGCCTGTTTCAGCTGCAACAGTTTGCGGC										
670	GCTTGCTGCCTTATTACTGACAGCGAGTAGCCTGTTTCAGCTGCAACAGTTTGCGGC										
6BF	GCTTGCTGCCTTATTACTGACAGCGAGTAGCCTGTTTCAGCTGCAACAGTTTGCGGC										
6BSP	GCTTGCTGCCTTATTACTGACAGCGAGTAGCCTGTTTCAGCTGCAACAGTTTGCGGC										
19AH	GCTTGCTGCCTTATTACTGACAGCGAGTAGCCTGTTTCAGCTGCAACAGTTTGCGGC										
23FPO	GCTTGCTGCCTTATTACTGACAGCGAGTAGCCTGTTTCAGCTGCAACAGTTTGCGGC										
19FTW	GCTTGCTGCCTTATTACTGACAGCGAGTAGCCTGTTTCAGCTGCAACAGTTTGCGGC										
9VSP	GCTTGCTGCCTTATTACTGACAGCGAGTAGCCTGTTTCAGCTGCAACAGTTTGCGGC										
TIGR4	GCTTGCTGCCTTATTACTGACAGCGAGTAGCCTGTTTCAGCTGCAACAGTTTGCGGC										
23FTW	ACTTGCTGCCTTATTACTGACAGTGAGTAGCCTGTTTCAGCTGCAACAGTTTGCGGC										

14CSR	GGACAATGTTAGTACAGCACCAGATGTTACTAAAACTTAACATCCATAAGTTACT										
670	GGACAATGTTAGTACAGCACCAGATGTTACTAAAACTTAACATCCATAAGTTACT										
6BF	GGACAATGTTAGTACAGCACCAGATGTTACTAAAACTTAACATCCATAAGTTACT										
6BSP	GGACAATGTTAGTACAGCACCAGATGTTACTAAAACTTAACATCCATAAGTTACT										
19AH	GGACAATGTTAGTACAGCACCAGATGTTACTAAAACTTAACATCCATAAGTTACT										
23FPO	GGACAATGTTAGTACAGCACCAGATGTTACTAAAACTTAACATCCATAAGTTACT										
19FTW	TGG-GACGACA--ACAACATCTGTTACCGTTACAAACTATTGGCAACAGATGGGGATAT										
9VSP	TGG-GACGACA--ACAACATCTGTTACCGTTACAAACTATTGGCAACAGATGGGGATAT										
TIGR4	TGG-GACGACA--ACAACATCTGTTACCGTTACAAACTATTGGCAACAGATGGGGATAT										
23FTW	GGA-AACAAA--ACTAACAGACACTTACAGTTACAAATTATTGATGACAGATCAAGAGCT										
	*	*	*	*	*	*	*	*	*	*	*
14CSR	GCTCTCA---GAAGATGATTTAAAGACTTGGGATACAAACGGCTCAA-AGGATATGATG										
670	GCTCTCA---GAAGATGATTTAAAGACTTGGGATACAAACGGCTCAA-AGGATATGATG										
6BF	GCTCTCA---GAAGATGATTTAAAGACTTGGGATACAAACGGCTCAA-AGGATATGATG										
6BSP	GCTCTCA---GAAGATGATTTAAAGACTTGGGATACAAACGGCTCAA-AGGATATGATG										
19AH	GCTCTCA---GAAGATGATTTAAAGACTTGGGATACAAACGGCTCAA-AGGATATGATG										
23FPO	GCTCTCA---GAAGATGATTTAAAGACTTGGGATACAAACGGCTCAA-AGGATATGATG										
19FTW	GGATAAAATGCAAATGAGTTAGAACAGGTAACATGCTGTTACAAATGCTGTTAC										
9VSP	GGATAAAATGCAAATGAGTTAGAACAGGTAACATGCTGTTACAAATGCTGTTAC										
TIGR4	GGATAAAATGCAAATGAGTTAGAACAGGTAACATGCTGTTACAAATGCTGTTAC										
23FTW	TGAC-----GCTTGGATTCTGATGCGATTACTACTGCGAGTTATGACGGTTCGAA										
	*	*	*	*	*	*	*	*	*	*	

Figure 196R

Figure 196S

PCT/US05/23236412/487

Figure 196T

PCT/US05/23239

413/487

14CSR	CTATGGATCAAGCTGATTATGAAGTCACTAAAGGAAATAATGGCTTAACCTTAAATTAA CTATGGATCAAGCTGATTATGAAGTCACTAAAGGAAATAATGGCTTAACCTTAAATTAA CTATGGATCAAGCTGATTATGAAGTCACTAAAGGAAATAATGGCTTAACCTTAAATTAA CTATGGATCAAGCTGATTATGAAGTCACTAAAGGAAATAATGGCTTAACCTTAAATTAA CTATGGATCAAGCTGATTATGAAGTCACTAAAGGAAAYTAATGGCTTAACCTTAAATTAA CTATGGATCAAGCTGATTATGAAGTCACTAAAGGAAATTATGGCTTAACCTTAAATTAA CACTTGAAGCAGGTGATTATGCTAACAGAAGTAGCAACTGGTTGATTTGAAATTAA CACTTGAAGCAGGTGATTATGCTAACAGAAGTAGCAACTGGTTGATTTGAAATTAA CACTTGAAGCAGGTGATTATGCTAACAGAAGTAGCAACTGGTTGATTTGAAATTAA CGCTTGATAATTCTCATTACACATTAGAACAGGTCATAATGGCTTATCTGAAAGTTAA *
14CSR	CAGAACGCAGGTTTAGCTAAAATTAAATGGTAAGGATGCAGACAAAAATCCAAATTACTT CAGAACGCAGGTTTAGCTAAAATTAAATGGTAAGGATGCAGACAAAAATCCAAATTACTT CAGAACGCAGGTTTAGCTAAAATTAAATGGTAAGGATGCAGACAAAAATCCAAATTACTT CAGAACGCAGGTTTAGCTAAAATTAAATGGTAAGGATGCAGACAAAAATCCAAATTACTT CAGAACGCAGGTTTAGCTAAAATTAAATGGTAAGGATGCAGACAAAAATCCAAATTACTT CAGATGCTGGTTAGCTAAAGTGAATGACCAAAACGCTGAAAAAAACTGTGAAATCATT CAGATGCTGGTTAGCTAAAGTGAATGACCAAAACGCTGAAAAAAACTGTGAAATCATT CAGATGCTGGTTAGCTAAAGTGAATGACCAAAACGCTGAAAAAAACTGTGAAATCATT ATGAAAAAGGCTGGAAGCAATCACGGTAAAGATGCAGAACACAATTACGTTGAAAGT *
14CSR	ACTCAGCTACTTTGAACTCACTTGCTGTTGCAGACATTCCCTGAAAGTAACGATATTACAT ACTCAGCTACTTTGAACTCACTTGCTGTTGCAGACATTCCCTGAAAGTAACGATATTACAT ACTCAGCTACTTTGAACACTCACTTGCTGTTGCAGACATTCCCTGAAAGTAACGATATTACAT ACTCAGCTACTTTGAACACTCACTTGCTGTTGCAGACATTCCCTGAAAGTAACGATATTACAT ACTCAGCTACTTTGAACACTCACTTGCTGTTGCAGACATTCCCTGAAAGTAACGATATTACAT ATTCCGCAACATTGAATGACAAAGCAATTGTTAGAAGTACCGAGAATCTAATGATGTAACAT ATTCCGCAACATTGAATGACAAAGCAATTGTTAGAAGTACCGAGAATCTAATGATGTAACAT ATTCCGCAACATTGAATGACAAAGCAATTGTTAGAAGTACCGAGAATCTAATGATGTAACAT ATTCCGCAACATTGAATGACAAAGCAATTGTTAGAAGTACCGAGAATCTAATGATGTAACAT *
14CSR	ATCATTACGAAATCATCAAGATCATGGGAATACTCCAAAACCAACTAAACC---TAATA ATCATTACGAAATCATCAAGATCATGGGAATACTCCAAAACCAACTAAACC---TAATA ATCATTACGAAATCATCAAGATCATGGGAATACTCCAAAACCAACTAAACC---TAATA ATCATTACGAAATCATCAAGATCATGGGAATACTCCAAAACCAACTAAACC---TAATA ATCATTACGAAATCATCAAGATCATGGGAATACTCCAAAACCAACTAAACC---TAATA TTAACTATGGTAATAATCCAGATCACGGGAATACTCCAAAGCGAATAAGCCAATGAAA TTAACTATGGTAATAATCCAGATCACGGGAATACTCCAAAGCGAATAAGCCAATGAAA TTAACTATGGTAATAATCCAGATCACGGGAATACTCCAAAGCGAATAAGCCAATGAAA TCCATTATGGAAACAACCCAGGTCACTGGTAACACTCCAAAACCAACAAACC---TAAAA *
14CSR	ATGGTCAAATTACAGTAACTAAAGACATGGG-----ACAGTCA-ACCTGCTCCTGAGG ATGGTCAAATTACAGTAACTAAAGACATGGG-----ACAGTCA-ACCTGCTCCTGAGG ATGGTCAAATTACAGTAACTAAAGACATGGG-----ACAGTCA-ACCTGCTCCTGAGG ATGGTCAAATTACAGTAACTAAAGACATGGG-----ACAGTCA-ACCTGCTCCTGAGG ATGGTCAAATTACAGTAACTAAAGACATGGG-----ACAGTCA-ACCTGCTCCTGAGG ATGGTCAAATTACAGTAACTAAAGACATGGG-----ACAGTCA-ACCTGCTCCTGAGG ACGGCGATTTGACATTGACCAAGACATGGGTTGATGCTACAGGTGCACCAATTCCGGCTG ACGGCGATTTGACATTGACCAAGACATGGGTTGATGCTACAGGTGCACCAATTCCGGCTG ACGGTGAACCTACAATTACTAAACATGGGCTGATGCTAAAGATGCTCCTAT---AGCAG *

Figure 196U

PCT/US05/27239

414/487

Figure 196V

PCT2US05/22222339

Figure 196W

PCT/US05/27239 416/487

Figure 196X

PCT/LJSDS/E27239 417/487

14CSR TGTTAAAAACAACAAAGATGAGGATCAACTTGCTTAAGTAAGAGAGAAAGGAGCCATTGA
 670 TGTTAAAAACAACAAAGATGAGGATCAACTTGCTTAAGTAAGAGAGAAAGGAGCCATTGA
 6BF TGTTAAAAACAACAAAGATGAGGATCAACTTGCTTAAGTAAGAGAGAAAGGAGCCATTGA
 6BSP TGTTAAAAACAACAAAGATGAGGATCAACTTGCTTAAGTAAGAGAGAAAGGAGCCATTGA
 19AH TGTTAAAAACAACAAAGATGAGGATCAACTTGCTTAAGTAAGAGAGAAAGGAGCCATTGA
 23FPO TGTTAAAAACAACAAAGATGAGGATCAACTTGCTTAAGTAAGAGAGAAAGGAGCCATTGA
 19FTW TGTTAAAAACAACAAAGATGAGGATCAACTTGCTTAAGTAAGAGAGAAAGGAGCCATTGA
 9VSP TGTTAAAAACAACAAAGATGAGGATCAACTTGCTTAAGTAAGAGAGAAAGGAGCCATTGA
 TIGR4 TGTTAAAAACAACAAAGATGAGGATCAACTTGCTTAAGTAAGAGAGAAAGGAGCCATTGA
 23FTW TGTTAAAAACAACAAAGATGAGGATCAACTTGCTTAAGTAAGAGAGAAAGGAGCCATTGA

 14CSR TGACAATGCAGAAAATGCAGAAAATG-----
 670 TGACAATGCAGAAAATGCAGAAAATG-----
 6BF TGACAATGCAGAAAATGCAGAAAATG-----
 6BSP TGACAATGCAGAAAATGCAGAAAATG-----
 19AH TGACAATGCAGAAAATGCAGAAAATG-----
 23FPO TGACAATGCAGAAAATGCAGAAAATG-----
 19FTW TGACAATGCAGAAAATGCAGAAAATG-----
 9VSP TGACAATGCAGAAAATGCAGAAAATG-----
 TIGR4 TGACAATGCAGAAAATGCAGAAAATG-----
 23FTW TGACAATGCAGAAAATGCAGAAAATG-----

 14CSR --ATTAGCTGTATCTCTTGTATGGCTCTGTGTTTCTTGTATGGGTGCACATG
 670 --ATTAGCTGTATCTCTTGTATGGCTCTGTGTTTCTTGTATGGGTGCACATG
 6BF --ATTAGCTGTATCTCTTGTATGGCTCTGTGTTTCTTGTATGGGTGCACATG
 6BSP --ATTAGCTGTATCTCTTGTATGGCTCTGTGTTTCTTGTATGGGTGCACATG
 19AH --ATTAGCTGTATCTCTTGTATGGCTCTGTGTTTCTTGTATGGGTGCACATG
 23FPO --ATTAGCTGTATCTCTTGTATGGCTCTGTGTTTCTTGTATGGGTGCACATG
 19FTW --ATTAGCTGTATCTCTTGTATGGCTCTGTGTTTCTTGTATGGGTGCACATG
 9VSP --ATTAGCTGTATCTCTTGTATGGCTCTGTGTTTCTTGTATGGGTGCACATG
 TIGR4 --ATTAGCTGTATCTCTTGTATGGCTCTGTGTTTCTTGTATGGGTGCACATG
 23FTW --ATTAGCTGTATCTCTTGTATGGCTCTGTGTTTCTTGTATGGGTGCACATG

 14CSR CAGTCCAAGCGCAAGAAGATCACACGTTGGTCTTGCATTGGAGAACTATCAGGAGGTGG
 670 CAGTCCAAGCGCAAGAAGATCACACGTTGGTCTTGCATTGGAGAACTATCAGGAGGTGG
 6BF CAGTCCAAGCGCAAGAAGATCACACGTTGGTCTTGCATTGGAGAACTATCAGGAGGTGG
 6BSP CAGTCCAAGCGCAAGAAGATCACACGTTGGTCTTGCATTGGAGAACTATCAGGAGGTGG
 19AH CAGTCCAAGCGCAAGAAGATCACACGTTGGTCTTGCATTGGAGAACTATCAGGAGGTGG
 23FPO CAGTCCAAGCGCAAGAAGATCACACGTTGGTCTTGCATTGGAGAACTATCAGGAGGTGG
 19FTW CAGTCCAAGCGCAAGAAGATCACACGTTGGTCTTGCATTGGAGAACTATCAGGAGGTGG
 9VSP CAGTCCAAGCGCAAGAAGATCACACGTTGGTCTTGCATTGGAGAACTATCAGGAGGTGG
 TIGR4 CAGTCCAAGCGCAAGAAGATCACACGTTGGTCTTGCATTGGAGAACTATCAGGAGGTGG
 23FTW CAGTCCAAGCGCAAGAAGATCACACGTTGGTCTTGCATTGGAGAACTATCAGGAGGTGG

 14CSR TTAGTCATTGCCATCTCGTGATGGTCATCGGTGCAAGTATGGAAGTTGGATGATTGTT
 670 TTAGTCATTGCCATCTCGTGATGGTCATCGGTGCAAGTATGGAAGTTGGATGATTGTT
 6BF TTAGTCATTGCCATCTCGTGATGGTCATCGGTGCAAGTATGGAAGTTGGATGATTGTT
 6BSP TTAGTCATTGCCATCTCGTGATGGTCATCGGTGCAAGTATGGAAGTTGGATGATTGTT
 19AH TTAGTCATTGCCATCTCGTGATGGTCATCGGTGCAAGTATGGAAGTTGGATGATTGTT
 23FPO TTAGTCATTGCCATCTCGTGATGGTCATCGGTGCAAGTATGGAAGTTGGATGATTGTT
 19FTW TTAGTCATTGCCATCTCGTGATGGTCATCGGTGCAAGTATGGAAGTTGGATGATTGTT
 9VSP TTAGTCATTGCCATCTCGTGATGGTCATCGGTGCAAGTATGGAAGTTGGATGATTGTT
 TIGR4 TTAGTCATTGCCATCTCGTGATGGTCATCGGTGCAAGTATGGAAGTTGGATGATTGTT
 23FTW TTAGTCATTGCCATCTCGTGATGGTCATCGGTGCAAGTATGGAAGTTGGATGATTGTT

Figure 196Y

PCT/US05/237239 418/487

14CSR	ATTCCTATGATGATCGGGTGC AAATTGTAAGAGACTTGCATTG TGGGATGAGAATAAAC
670	ATTCCTATGATGATCGGGTGC AAATTGTAAGAGACTTGCATTG TGGGATGAGAATAAAC
6BF	ATTCCTATGATGATCGGGTGC AAATTGTAAGAGACTTGCATTG TGGGATGAGAATAAAC
6BSP	ATTCCTATGATGATCGGGTGC AAATTGTAAGAGACTTGCATTG TGGGATGAGAATAAAC
19AH	ATTCCTATGATGATCGGGTGC AAATTGTAAGAGACTTGCATTG TGGGATGAGAATAAAC
23FPO	ATTCCTATGATAATCGGGTGC AAATTGAGAGACTTGCATTG TGGGATGAGAATAAAC
19FTW	ATTCCTATGATAATCGGGTGC AAATTGAGAGACTTGCATTG TGGGATGAGAATAAAC
9VSP	ATTCCTATGATAATCGGGTGC AAATTGAGAGACTTGCATTG TGGGATGAGAATAAAC
TIGR4	ATTCCTATGATGATCGGGTGC AAATTGTAAGAGACTTGCATTG TGGGATGAGAATAAAC
23FTW	ATTCCTATGATAATCGGGTGC AAATTGAGAGACTTGCATTG TGGGATGAGAATAAAC

14CSR	TTTCTTCTTC AAAAAGACTTCGTTGAGATGACCTCCTTGAGAATCAGATTGAAGTAT
670	TTTCTTCTTC AAAAAGACTTCGTTGAGATGACCTCCTTGAGAATCAGATTGAAGTAT
6BF	TTTCTTCTTC AAAAAGACTTCGTTGAGATGACCTCCTTGAGAATCAGATTGAAGTAT
6BSP	TTTCTTCTTC AAAAAGACTTCGTTGAGATGACCTCCTTGAGAATCAGATTGAAGTAT
19AH	TTTCTTCTTC AAAAAGACTTCGTTGAGATGACCTCCTTGAGAATCAGATTGAAGTAT
23FPO	TTTCTTCTTC AAAAAGACTTCGTTGAGATGACCTCCTTGAGAATCAGATTGAAGTAT
19FTW	TTTCTTCTTC AAAAAGACTTCGTTGAGATGACCTCCTTGAGAATCAGATTGAAGTAT
9VSP	TTTCTTCTTC AAAAAGACTTCGTTGAGATGACCTCCTTGAGAATCAGATTGAAGTAT
TIGR4	TTTCTTCTTC AAAAAGACTTCGTTGAGATGACCTCCTTGAGAATCAGATTGAAGTAT
23FTW	TTTCTTCTTC AAAAAGACTTCGTTGAGATGACCTCCTTGAGAATCAGATTGAAGTAT

14CSR	CTCATATTCCAATGGCTTTACTATGTTGCTCTATTATCCAGACGGATGCGGTTTCTT
670	CTCATATTCCAATGGCTTTACTATGTTGCTCTATTATCCAGACGGATGCGGTTTCTT
6BF	CTCATATTCCAATGGCTTTACTATGTTGCTCTATTATCCAGACGGATGCGGTTTCTT
6BSP	CTCATATTCCAATGGCTTTACTATGTTGCTCTATTATCCAGACGGATGCGGTTTCTT
19AH	CTCATATTCCAATGGCTTTACTATGTTGCTCTATTATCCAGACGGATGCGGTTTCTT
23FPO	CTCATATTCCAATGGCTTTACTATGTTGCTCTATTATCCAGACGGATGCGGTTTCTT
19FTW	CTCATATTCCAATGGCTTTACTATGTTGCTCTATTATCCAGACGGATGCGGTTTCTT
9VSP	CTCATATTCCAATGGCTTTACTATGTTGCTCTATTATCCAGACGGATGCGGTTTCTT
TIGR4	CTCATATTCCAATGGCTTTACTATGTTGCTCTATTATCCAGACGGATGCGGTTTCTT
23FTW	CTCATATTCCAATGGCTTTACTATGTTGCTCTATTATCCAGACGGATGCGGTTTCTT

14CSR	ATCCAGCTGA ATTCTTTGAAATGACAGATCAAACGGTAGAGCCTTGGTCATTGTAG
670	ATCCAGCTGA ATTCTTTGAAATGACAGATCAAACGGTAGAGCCTTGGTCATTGTAG
6BF	ATCCAGCTGA ATTCTTTGAAATGACAGATCAAACGGTAGAGCCTTGGTCATTGTAG
6BSP	ATCCAGCTGA ATTCTTTGAAATGACAGATCAAACGGTAGAGCCTTGGTCATTGTAG
19AH	ATCCAGCTGA ATTCTTTGAAATGACAGATCAAACGGTAGAGCCTTGGTCATTGTAG
23FPO	ATCCAGCTGA ATTCTTTGAAATGACAGATCAAACGGTAGAGCCTTGGTCATTGTAG
19FTW	ATCCAGCTGA ATTCTTTGAAATGACAGATCAAACGGTAGAGCCTTGGTCATTGTAG
9VSP	ATCCAGCTGA ATTCTTTGAAATGACAGATCAAACGGTAGAGCCTTGGTCATTGTAG
TIGR4	ATCCAGCTGA ATTCTTTGAAATGACAGATCAAACGGTAGAGCCTTGGTCATTGTAG
23FTW	ATCCAGCTGA ATTCTTTGAAATGACAGATCAAACGGTAGAGCCTTGGTCATTGTAG

14CSR	CGAAAAAAACAGATACAATGACAACAAAGGTGAAGCTGATAAAGGTGGATCAAGACCACA
670	CGAAAAAAACAGATACAATGACAACAAAGGTGAAGCTGATAAAGGTGGATCAAGACCACA
6BF	CGAAAAAAACAGATACAATGACAACAAAGGTGAAGCTGATAAAGGTGGATCAAGACCACA
6BSP	CGAAAAAAACAGATACAATGACAACAAAGGTGAAGCTGATAAAGGTGGATCAAGACCACA
19AH	CGAAAAAAACAGATACAATGACAACAAAGGTGAAGCTGATAAAGGTGGATCAAGACCACA
23FPO	CGAAAAAAACAGATACGGTACAACAAAGGTGAAGCTGATAAAGGTGGATCAAGACCACA
19FTW	CGAAAAAAACAGATACGGTACAACAAAGGTGAAGCTGATAAAGGTGGATCAAGACCACA
9VSP	CGAAAAAAACAGATACGGTACAACAAAGGTGAAGCTGATAAAGGTGGATCAAGACCACA
TIGR4	CGAAAAAAACAGATACGGTACAACAAAGGTGAAGCTGATAAAGGTGGATCAAGACCACA
23FTW	CGAAAAAAACAGATACGGTACAACAAAGGTGAAGCTGATAAAGGTGGATCAAGACCACA

Figure 196X

14CSR	ATCGCTTGGAGGGTGTGGCTTTAAATTGGTATCAGTAGCAAGAGATGGTTCTGAAAAAG
670	ATCGCTTGGAGGGTGTGGCTTTAAATTGGTATCAGTAGCAAGAGATGGTTCTGAAAAAG
6BF	ATCGCTTGGAGGGTGTGGCTTTAAATTGGTATCAGTAGCAAGAGATGGTTCTGAAAAAG
6BSP	ATCGCTTGGAGGGTGTGGCTTTAAATTGGTATCAGTAGCAAGAGATGGTTCTGAAAAAG
19AH	ATCGCTTGGAGGGTGTGGCTTTAAATTGGTATCAGTAGCAAGAGATGGTTCTGAAAAAG
23FPO	ATCGCTTGGAGGGTGTGGCTTTAAATTGGTATCAGTAGCAAGAGATGGTTCTGAAAAAG
19FTW	ATCGCTTGGAGGGTGTGGCTTTAAATTGGTATCAGTAGCAAGAGATGGTTCTGAAAAAG
9VSP	ATCGCTTGGAGGGTGTGGCTTTAAATTGGTATCAGTAGCAAGAGATGGTTCTGAAAAAG
TIGR4	ATCGCTTGGAGGGTGTGGCTTTAAATTGGTATCAGTAGCAAGAGATGGTTCTGAAAAAG
23FTW	ATCGCTTGGAGGGTGTGGCTTTAAATTGGTATCAGTAGCAAGAGATGGTTCTGAAAAAG

14CSR	AGGTTCCCTGATTGGAGAATACCGTTACAGTTCTCTGGTCAAGTAGGGAGAACTCTCT
670	AGGTTCCCTGATTGGAGAATACCGTTACAGTTCTCTGGTCAAGTAGGGAGAACTCTCT
6BF	AGGTTCCCTGATTGGAGAATACCGTTACAGTTCTCTGGTCAAGTAGGGAGAACTCTCT
6BSP	AGGTTCCCTGATTGGAGAATACCGTTACAGTTCTCTGGTCAAGTAGGGAGAACTCTCT
19AH	AGGTTCCCTGATTGGAGAATACCGTTACAGTTCTCTGGTCAAGTAGGGAGAACTCTCT
23FPO	AGGTTCCCTGATTGGAGAATACCGTTACAGTTCTCTGGTCAAGTAGGGAGAACTCTCT
19FTW	AGGTTCCCTGATTGGAGAATACCGTTACAGTTCTCTGGTCAAGTAGGGAGAACTCTCT
9VSP	AGGTTCCCTGATTGGAGAATACCGTTACAGTTCTCTGGTCAAGTAGGGAGAACTCTCT
TIGR4	AGGTTCCCTGATTGGAGAATACCGTTACAGTTCTCTGGTCAAGTAGGGAGAACTCTCT
23FTW	AGGTTCCCTGATTGGAGAATACCGTTACAGTTCTCTGGTCAAGTAGGGAGAACTCTCT

14CSR	ATACTGATAAAAATGGAGAGATTTTGTGACAATCTCCTTGGGAACTATCGTTCA
670	ATACTGATAAAAATGGAGAGATTTTGTGACAATCTCCTTGGGAACTATCGTTCA
6BF	ATACTGATAAAAATGGAGAGATTTTGTGACAATCTCCTTGGGAACTATCGTTCA
6BSP	ATACTGATAAAAATGGAGAGATTTTGTGACAATCTCCTTGGGAACTATCGTTCA
19AH	ATACTGATAAAAATGGAGAGATTTTGTGACAATCTCCTTGGGAACTATCGTTCA
23FPO	ATACTGATAAAAATGGAGAGATTTTGTGACAATCTCCTTGGGAACTATCGTTCA
19FTW	ATACTGATAAAAATGGAGAGATTTTGTGACAATCTCCTTGGGAACTATCGTTCA
9VSP	ATACTGATAAAAATGGAGAGATTTTGTGACAATCTCCTTGGGAACTATCGTTCA
TIGR4	ATACTGATAAAAATGGAGAGATTTTGTGACAATCTCCTTGGGAACTATCGTTCA
23FTW	ATACTGATAAAAATGGAGAGATTTTGTGACAATCTCCTTGGGAACTATCGTTCA

14CSR	AGGAGGTGGAGCCACTGGCAGGCATGCTTACGACGCTGGATACGGATGTCCAGCTGG
670	AGGAGGTGGAGCCACTGGCAGGCATGCTTACGACGCTGGATACGGATGTCCAGCTGG
6BF	AGGAGGTGGAGCCACTGGCAGGCATGCTTACGACGCTGGATACGGATGTCCAGCTGG
6BSP	AGGAGGTGGAGCCACTGGCAGGCATGCTTACGACGCTGGATACGGATGTCCAGCTGG
19AH	AGGAGGTGGAGCCACTGGCAGGCATGCTTACGACGCTGGATACGGATGTCCAGCTGG
23FPO	AGGAGGTGGAGCCACTGGCAGGCATGCTTACGACGCTGGATACGGATGTCCAGCTGG
19FTW	AGGAGGTGGAGCCACTGGCAGGCATGCTTACGACGCTGGATACGGATGTCCAGCTGG
9VSP	AGGAGGTGGAGCCACTGGCAGGCATGCTTACGACGCTGGATACGGATGTCCAGCTGG
TIGR4	AGGAGGTGGAGCCACTGGCAGGCATGCTTACGACGCTGGATACGGATGTCCAGCTGG
23FTW	AGGAGGTGGAGCCACTGGCAGGCATGCTTACGACGCTGGATACGGATGTCCAGCTGG

14CSR	TAGATCATCAGCTGGTGACGATTACGGTTGTCATCAGAAATTACACGTGGCAATGTTG
670	TAGATCATCAGCTGGTGACGATTACGGTTGTCATCAGAAATTACACGTGGCAATGTTG
6BF	TAGATCATCAGCTGGTGACGATTACGGTTGTCATCAGAAATTACACGTGGCAATGTTG
6BSP	TAGATCATCAGCTGGTGACGATTACGGTTGTCATCAGAAATTACACGTGGCAATGTTG
19AH	TAGATCATCAGCTGGTGACGATTACGGTTGTCATCAGAAATTACACGTGGCAATGTTG
23FPO	TAGATCATCAGCTGGTGACGATTACGGTTGTCATCAGAAATTACACGTGGCAATGTTG
19FTW	TAGATCATCAGCTGGTGACGATTACGGTTGTCATCAGAAATTACACGTGGCAATGTTG
9VSP	TAGATCATCAGCTGGTGACGATTACGGTTGTCATCAGAAATTACACGTGGCAATGTTG
TIGR4	TAGATCATCAGCTGGTGACGATTACGGTTGTCATCAGAAATTACACGTGGCAATGTTG
23FTW	TAGATCATCAGCTGGTGACGATTACGGTTGTCATCAGAAATTACACGTGGCAATGTTG

Figure 196AA

PCT/US05/27239 420/487

14CSR	ACTTTATGAAGGTGGATGGTCGGACCAATACTCTCTTCAAGGGGCAATGTTCAAAGTCA
670	ACTTTATGAAGGTGGATGGTCGGACCAATACTCTCTTCAAGGGGCAATGTTCAAAGTCA
6BF	ACTTTATGAAGGTGGATGGTCGGACCAATACTCTCTTCAAGGGGCAATGTTCAAAGTCA
6BSP	ACTTTATGAAGGTGGATGGTCGGACCAATACTCTCTTCAAGGGGCAATGTTCAAAGTCA
19AH	ACTTTATGAAGGTGGATGGTCGGACCAATACTCTCTTCAAGGGGCAATGTTCAAAGTCA
23FPO	ACTTTATGAAGGTGGATGGTAGGACCAATACTCTCTTCAAGGGGCAATGTTCAAAGTCA
19FTW	ACTTTATGAAGGTGGATGGTAGGACCAATACTCTCTTCAAGGGGCAATGTTCAAAGTCA
9VSP	ACTTTATGAAGGTGGATGGTAGGACCAATACTCTCTTCAAGGGGCAATGTTCAAAGTCA
TIGR4	ACTTTATGAAGGTGGATGGTCGGACCAATACTCTCTTCAAGGGGCAATGTTCAAAGTCA
23FTW	ACTTTATGAAGGTGGATGGTCGGACCAATACTCTCTTCAAGGGGCAATGTTCAAAGTCA

14CSR	TGAAAAGAAGAAAGCGGACACTATACTCCTGTTCTTCAAAATGTAAGGAAGTAGTTGTAA
670	TGAAAAGAAGAAAGCGGACACTATACTCCTGTTCTTCAAAATGTAAGGAAGTAGTTGTAA
6BF	TGAAAAGAAGAAAGCGGACACTATACTCCTGTTCTTCAAAATGTAAGGAAGTAGTTGTAA
6BSP	TGAAAAGAAGAAAGCGGACACTATACTCCTGTTCTTCAAAATGTAAGGAAGTAGTTGTAA
19AH	TGAAAAGAAGAAAGCGGACACTATACTCCTGTTCTTCAAAATGTAAGGAAGTAGTTGTAA
23FPO	TGAAAAGAAGAAACCGGACACTATACTCCTGTTCTTCAAAATGTAAGGAAGTAGTTGTGG
19FTW	TGAAAAGAAGAAACCGGACACTATACTCCTGTTCTTCAAAATGTAAGGAAGTAGTTGTGG
9VSP	TGAAAAGAAGAAACCGGACACTATACTCCTGTTCTTCAAAATGTAAGGAAGTAGTTGTGG
TIGR4	TGAAAAGAAGAAACCGGACACTATACTCCTGTTCTTCAAAATGTAAGGAAGTAGTTGTGG
23FTW	TGAAAAGAAGAAACCGGACACTATACTCCTGTTCTTCAAAATGTAAGGAAGTAGTTGTGG

14CSR	CATCAGGGAAAAGATGGTCGTTCCGAGTGGAAAGGTCTAGAGTATGGGACATACTATTAT
670	CATCAGGGAAAAGATGGTCGTTCCGAGTGGAAAGGTCTAGAGTATGGGACATACTATTAT
6BF	CATCAGGGAAAAGATGGTCGTTCCGAGTGGAAAGGTCTAGAGTATGGGACATACTATTAT
6BSP	CATCAGGGAAAAGATGGTCGTTCCGAGTGGAAAGGTCTAGAGTATGGGACATACTATTAT
19AH	CATCAGGGAAAAGATGGTCGTTCCGAGTGGAAAGGTCTAGAGTATGGGACATACTATTAT
23FPO	CATCAGGGAAAAGATGGTCGTTCCGAGTGGAAAGGTCTAGAGTATGGGACATACTATTAT
19FTW	CATCAGGGAAAAGATGGTCGTTCCGAGTGGAAAGGTCTAGAGTATGGGACATACTATTAT
9VSP	CATCAGGGAAAAGATGGTCGTTCCGAGTGGAAAGGTCTAGAGTATGGGACATACTATTAT
TIGR4	CATCAGGGAAAAGATGGTCGTTCCGAGTGGAAAGGTCTAGAGTATGGGACATACTATTAT
23FTW	CATCAGGGAAAAGATGGTCGTTCCGAGTGGAAAGGTCTAGAGTATGGGACATACTATTAT

14CSR	GGGAGCTCCAAGCTCCAACGGTTATGTTCAATTAAACATGCCCTGTTCTTACAATCG
670	GGGAGCTCCAAGCTCCAACGGTTATGTTCAATTAAACATGCCCTGTTCTTACAATCG
6BF	GGGAGCTCCAAGCTCCAACGGTTATGTTCAATTAAACATGCCCTGTTCTTACAATCG
6BSP	GGGAGCTCCAAGCTCCAACGGTTATGTTCAATTAAACATGCCCTGTTCTTACAATCG
19AH	GGGAGCTCCAAGCTCCAACGGTTATGTTCAATTAAACATGCCCTGTTCTTACAATCG
23FPO	GGGAGCTCCAAGCTCCAACGGTTATGTTCAATTAAACATGCCCTGTTCTTACAATCG
19FTW	GGGAGCTCCAAGCTCCAACGGTTATGTTCAATTAAACATGCCCTGTTCTTACAATCG
9VSP	GGGAGCTCCAAGCTCCAACGGTTATGTTCAATTAAACATGCCCTGTTCTTACAATCG
TIGR4	GGGAGCTCCAAGCTCCAACGGTTATGTTCAATTAAACATGCCCTGTTCTTACAATCG
23FTW	GGGAGCTCCAAGCTCCAACGGTTATGTTCAATTAAACATGCCCTGTTCTTACAATCG

14CSR	GGAAAGATACTCGTAAGGAACGGTAAACAGTGGTAAAAATAACAAGCGACCACGGATTG
670	GGAAAGATACTCGTAAGGAACGGTAAACAGTGGTAAAAATAACAAGCGACCACGGATTG
6BF	GGAAAGATACTCGTAAGGAACGGTAAACAGTGGTAAAAATAACAAGCGACCACGGATTG
6BSP	GGAAAGATACTCGTAAGGAACGGTAAACAGTGGTAAAAATAACAAGCGACCACGGATTG
19AH	GGAAAGATACTCGTAAGGAACGGTAAACAGTGGTAAAAATAACAAGCGACCACGGATTG
23FPO	GGAAAGATACTCGTAAGGAACGGTAAACAGTGGTAAAAATAACAAGCGACCACGGATTG
19FTW	GGAAAGATACTCGTAAGGAACGGTAAACAGTGGTAAAAATAACAAGCGACCACGGATTG
9VSP	GGAAAGATACTCGTAAGGAACGGTAAACAGTGGTAAAAATAACAAGCGACCACGGATTG
TIGR4	GGAAAGATACTCGTAAGGAACGGTAAACAGTGGTAAAAATAACAAGCGACCACGGATTG
23FTW	GGAAAGATACTCGTAAGGAACGGTAAACAGTGGTAAAAATAACAAGCGACCACGGATTG

Figure 196AB

14CSR ATGTGCCAGATAACAGGGGAAGAAAACCTTGATATCTTGTGCTTGCCTTTGTGT
 670 ATGTGCCAGATAACAGGGGAAGAAAACCTTGATATCTTGTGCTTGCCTTTGTGT
 6BF ATGTGCCAGATAACAGGGGAAGAAAACCTTGATATCTTGTGCTTGCCTTTGTGT
 6BSP ATGTGCCAGATAACAGGGGAAGAAAACCTTGATATCTTGTGCTTGCCTTTGTGT
 19AH ATGTGCCAGATAACAGGGGAAGAAAACCTTGATATCTTGTGCTTGCCTTTGTGT
 23FPO ATGTGCCAGATAACAGGGGAAGAAAACCTTGATATCTTGTGCTTGCCTTTGTGT
 19FTW ATGTGCCAGATAACAGGGGAAGAAAACCTTGATATCTTGTGCTTGCCTTTGTGT
 9VSP ATGTGCCAGATAACAGGGGAAGAAAACCTTGATATCTTGTGCTTGCCTTTGTGT
 TIGR4 ATGTGCCAGATAACAGGGGAAGAAAACCTTGATATCTTGTGCTTGCCTTTGTGT
 23FTW ATGTGCCAGATAACAGGGGAAGAAAACCTTGATATCTTGTGCTTGCCTTTGTGT

 14CSR TTGGTAGTGGTTATTATCTACGAAAAAACCAAATAACTGATATTCAATGTACATCATTAA
 670 TTGGTAGTGGTTATTATCTACGAAAAAACCAAATAACTGATATTCAATGTACATCATTAA
 6BF TTGGTAGTGGTTATTATCTACGAAAAAACCAAATAACTGATATTCAATGTACATCATTAA
 6BSP TTGGTAGTGGTTATTATCTACGAAAAAACCAAATAACTGATATTCAATGTACATCATTAA
 19AH TTGGTAGTGGTTATTATCTACGAAAAAACCAAATAACTGATATTCAATGTACATCATTAA
 23FPO TTGGTAGTGGCTTATTATCTACGAAAAAACCAAATAACTGATATTCAATGTACATCATTAA
 19FTW TTGGTAGTGGCTTATTATCTACGAAAAAACCAAATAACTGATATTCAATGTACATCATTAA
 9VSP TTGGTAGTGGCTTATTATCTACGAAAAAACCAAATAACTGATATTCAATGTACATCATTAA
 TIGR4 TTGGTAGTGGCTTATTATCTACGAAAAAACCAAATAACTGATATTCAATGTACATCATTAA
 23FTW TTGGTAGTGGCTTATTATCTACGAAAAAACCAAATAACTGATATTCAATGTACATCATTAA

 14CSR TGAAAAAGATAGCAGGCTGAAGGGAGACGAGACTCTGAGGTGATGTTAATCAGGAA
 670 TGAAAAAGATAGCAGGCTGAAGGGAGACGAGACTCTGAGGTGATGTTAATCAGGAA
 6BF TGAAAAAGATAGCAGGCTGAAGGGAGACGAGACTCTGAGGTGATGTTAATCAGGAA
 6BSP TGAAAAAGATAGCAGGCTGAAGGGAGACGAGACTCTGAGGTGATGTTAATCAGGAA
 19AH TGAAAAAGATAGCAGGCTGAAGGGAGACGAGACTCTGAGGTGATGTTAATCAGGAA
 23FPO TGAAAAAGATAGCAGGCTGAAGGGAGACGAGACTCTGAGGTGATGTTAATCAGGAA
 19FTW TGAAAAAGATAGCAGGCTGAAGGGAGACGAGACTCTGAGGTGATGTTAATCAGGAA
 9VSP TGAAAAAGATAGCAGGCTGAAGGGAGACGAGACTCTGAGGTGATGTTAATCAGGAA
 TIGR4 TGAAAAAGATAGCAGGCTGAAGGGAGACGAGACTCTGAGGTGATGTTAATCAGGAA
 23FTW TGAAAAAGATAGCAGGCTGAAGGGAGACGAGACTCTGAGGTGATGTTAATCAGGAA

 14CSR TCATGGTAGTGGCATGAATCACATAACGGATATGAGGTGGCAGATTGTGCCAGCC
 670 TCATGGTAGTGGCATGAATCACATAACGGATATGAGGTGGCAGATTGTGCCAGCC
 6BF TCATGGTAGTGGCATGAATCACATAACGGATATGAGGTGGCAGATTGTGCCAGCC
 6BSP TCATGGTAGTGGCATGAATCACATAACGGATATGAGGTGGCAGATTGTGCCAGCC
 19AH TCATGGTAGTGGCATGAATCACATAACGGATATGAGGTGGCAGATTGTGCCAGCC
 23FPO TCATGGTAGTGGCATGAATCACATAACGGATATGAGGTGGCAGATTGTGCCAGCC
 19FTW TCATGGTAGTGGCATGAATCACATAACGGATATGAGGTGGCAGATTGTGCCAGCC
 9VSP TCATGGTAGTGGCATGAATCACATAACGGATATGAGGTGGCAGATTGTGCCAGCC
 TIGR4 TCATGGTAGTGGCATGAATCACATAACGGATATGAGGTGGCAGATTGTGCCAGCC
 23FTW TCATGGTAGTGGCATGAATCACATAACGGATATGAGGTGGCAGATTGTGCCAGCC

 14CSR TCATTGTGGTTATTGTTGTAACCGATAGGACTGGTCTGGAATCATTAGGAATGG
 670 TCATTGTGGTTATTGTTGTAACCGATAGGACTGGTCTGGAATCATTAGGAATGG
 6BF TCATTGTGGTTATTGTTGTAACCGATAGGACTGGTCTGGAATCATTAGGAATGG
 6BSP TCATTGTGGTTATTGTTGTAACCGATAGGACTGGTCTGGAATCATTAGGAATGG
 19AH TCATTGTGGTTATTGTTGTAACCGATAGGACTGGTCTGGAATCATTAGGAATGG
 23FPO TCATTGTGGTTATTGTTGTAACCGATAGGACTGGTCTGGAATCATTAGGAATGG
 19FTW TCATTGTGGTTATTGTTGTAACCGATAGGACTGGTCTGGAATCATTAGGAATGG
 9VSP TCATTGTGGTTATTGTTGTAACCGATAGGACTGGTCTGGAATCATTAGGAATGG
 TIGR4 TCATTGTGGTTATTGTTGTAACCGATAGGACTGGTCTGGAATCATTAGGAATGG
 23FTW TCATTGTGGTTATTGTTGTAACCGATAGGACTGGTCTGGAATCATTAGGAATGG

Figure 196AC

```

14CSR          ACAGGACTGGGATTCTGATTTAAAATGGATGGTGAATCAGAAAGAAAATGAGATTTCTCG
670           ACAGGACTGGGATTCTGATTTAAAATGGATGGTGAATCAGAAAGAAAATGAGATTTCTCG
6BF            ACAGGACTGGGATTCTGATTTAAAATGGATGGTGAATCAGAAAGAAAATGAGATTTCTCG
6BSP           ACAGGACTGGGATTCTGATTTAAAATGGATGGTGAATCAGAAAGAAAATGAGATTTCTCG
19AH           ACAGGACTGGGATTCTGATTTAAAATGGATGGTGAATCAGAAAGAAAATGAGATTTCTCG
23FPO          ACAGGACTGGGATTCTGATTTAAAATGGATGGTGAATCAGAAAGAAAATGAGATTTCTCG
19FTW          ACAGGACTGGGATTCTGATTTAAAATGGATGGTGAATCAGAAAGAAAATGAGATTTCTCG
9VSP           ACAGGACTGGGATTCTGATTTAAAATGGATGGTGAATCAGAAAGAAAATGAGATTTCTCG
TIGR4          ACAGGACTGGGATTCTGATTTAAAATGGATGGTGAATCAGAAAGAAAATGAGATTTCTCG
23FTW          ACAGGACTGGGATTCTGATTTAAAATGGATGGTGAATCAGAAAGAAAATGAGATTTCTCG
*****          *****
14CSR          TTTCTCTTAGCAGATAGGATTGTCGTAGGAAAAGCGATAAAATGATGAGTTGAAGAT
670           TTTCTCTTAGCAGATAGGATTGTCGTAGGAAAAGCGATAAAATGATGAGTTGAAGAT
6BF            TTTCTCTTAGCAGATAGGATTGTCGTAGGAAAAGCGATAAAATGATGAGTTGAAGAT
6BSP           TTTCTCTTAGCAGATAGGATTGTCGTAGGAAAAGCGATAAAATGATGAGTTGAAGAT
19AH           TTTCTCTTAGCAGATAGGATTGTCGTAGGAAAAGCGATAAAATGATGAGTTGAAGAT
23FPO          TTTCTCTTAGCAGATAGGATTGTCGTAGGAAAAGCGATAAAATGATGAGTTGAAGAT
19FTW          TTTCTCTTAGCAGATAGGATTGTCGTAGGAAAAGCGATAAAATGATGAGTTGAAGAT
9VSP           TTTCTCTTAGCAGATAGGATTGTCGTAGGAAAAGCGATAAAATGATGAGTTGAAGAT
TIGR4          TTTCTCTTAGCAGATAGGATTGTCGTAGGAAAAGCGATAAAATGATGAGTTGAAGAT
23FTW          TTTCTCTTAGCAGATAGGATTGTCGTAGGAAAAGCGATAAAATGATGAGTTGAAGAT
*****          *****
14CSR          AAAGGGATGCTGATAAAAA-TGGTAAAAACAAAAAGCAAATAATCTCCTATT
670           AAAGGGATGCTGATAAAAA-TGGTAAAAACAAAAAGCAAATAATCTCCTATT
6BF            AAAGGGATGCTGATAAAAA-TGGTAAAAACAAAAAGCAAATAATCTCCTATT
6BSP           AAAGGGATGCTGATAAAAA-TGGTAAAAACAAAAAGCAAATAATCTCCTATT
19AH           AAAGGAATGCTGATAAAAATGGCAAAAACAAAAAGCAAACAAATCTCCTATT
23FPO          AAAGGAATGCTGATAAAAATGGCAAAAACAAAAAGCAAACAAATCTCCTATT
19FTW          AAAGGAATGCTGATAAAAATGGCAAAAACAAAAAGCAAACAAATCTCCTATT
9VSP           AAAGGGATGCTGATAAAAA-TGGTAAAAACAAAAAGCAAATAATCTCCTATT
TIGR4          AAAGGGATGCTGATAAAAA-TGGTAAAAACAAAAAGCAAATAATCTCCTATT
23FTW          AAAGGGATGCTGATAAAAA-TGGTAAAAACAAAAAGCAAATAATCTCCTATT
*****          *****
14CSR          AGGAGTGGTATTTTCACTGGAAATGGCGGTAAATGGCGTATCCGTGGTGTCTCGCTTGTA
670           AGGAGTGGTATTTTCACTGGAAATGGCGGTAAATGGCGTATCCGTGGTGTCTCGCTTGTA
6BF            AGGAGTGGTATTTTCACTGGAAATGGCGGTAAATGGCGTATCCGTGGTGTCTCGCTTGTA
6BSP           AGGAGTGGTATTTTCACTGGAAATGGCGGTAAATGGCGTATCCGTGGTGTCTCGCTTGTA
19AH           AGGAGTGGTATTTTCACTGGAAATGGCGGTAAATGGCGTATCCGTGGTGTCTCGCTTGTA
23FPO          AGGAGTGGTATTTTCACTGGAAATGGCGGTAAATGGCGTATCCGTGGTGTCTCGCTTGTA
19FTW          AGGAGTGGTATTTTCACTGGAAATGGCGGTAAATGGCGTATCCGTGGTGTCTCGCTTGTA
9VSP           AGGAGTGGTATTTTCACTGGAAATGGCGGTAAATGGCGTATCCGTGGTGTCTCGCTTGTA
TIGR4          AGGAGTGGTATTTTCACTGGAAATGGCGGTAAATGGCGTATCCGTGGTGTCTCGCTTGTA
23FTW          AGGAGTGGTATTTTCACTGGAAATGGCGGTAAATGGCGTATCCGTGGTGTCTCGCTTGTA
*****          *****
14CSR          TTATCGAGTGGAAATCAAATCAACAAATTGCTGACTTTGATAAGGAAAAGCAAACGTTGGA
670           TTATCGAGTGGAAATCAAATCAACAAATTGCTGACTTTGATAAGGAAAAGCAAACGTTGGA
6BF            TTATCGAGTGGAAATCAAATCAACAAATTGCTGACTTTGATAAGGAAAAGCAAACGTTGGA
6BSP           TTATCGAGTGGAAATCAAATCAACAAATTGCTGACTTTGATAAGGAAAAGCAAACGTTGGA
19AH           TTATCGAGTGGAAATCAAATCAACAAATTGCTGACTTTGATAAGGAAAAGCAAACGTTGGA
23FPO          TTATCGAGTGGAAATCAAATCAACAAATTGCTGACTTTGATAAGGAAAAGCAAACGTTGGA
19FTW          TTATCGAGTGGAAATCAAATCAACAAATTGCTGACTTTGATAAGGAAAAGCAAACGTTGGA
9VSP           TTATCGAGTGGAAATCAAATCAACAAATTGCTGACTTTGATAAGGAAAAGCAAACGTTGGA
TIGR4          TTATCGAGTGGAAATCAAATCAACAAATTGCTGACTTTGATAAGGAAAAGCAAACGTTGGA
23FTW          TTATCGAGTGGAAATCAAATCAACAAATTGCTGACTTTGATAAGGAAAAGCAAACGTTGGA
*****          *****

```

Figure 196AD

PCT/US505/2723 423/487

Figure 196AE

PCT/US05/27239 424/487

Figure 196AF

Figure 196AG

Figure 196AH

PCT/US05/237239 427/487

14CSR	CTCATAGAGGATTACCGACGGCAGAACTGTTAGTCATTGGATAAGATGAAAAAAGGGG
670	CTCATAGAGGATTACCGACGGCAGAACTGTTAGTCATTGGATAAGATGAAAAAAGGGG
6BF	CTCATAGAGGATTACCGACGGCAGAACTGTTAGTCATTGGATAAGATGAAAAAAGGGG
6BSP	CTCATAGAGGATTACCGACGGCAGAACTGTTAGTCATTGGATAAGATGAAAAAAGGGG
19AH	CTCATAGAGGATTACCGACGGCAGAACTGTTAGTCATTGGATAAGATGAAAAAAGGGG
23FPO	CTCATAGAGGATTACCGACGGCAGAACTGTTAGTCATTGGATAAGATGAAAAAAGGGG
19FTW	CTCACAGAGGATTGCCAACGGCAGAACTGTTAGTCATTGGATAAGATGAAAAAAGGGG
9VSP	CTCATAGAGGATTACCGACGGCAGAACTGTTAGTCATTGGATAAGATGAAAAAAGGGG
TIGR4	CTCACAGAGGATTGCCAACGGCAGAACTGTTAGTCATTGGATAAGATGAAAAAAGGGG
23FTW	CTCATAGAGGATTACCGACGGCAGAACTGTTAGTCATTGGATAAGATGAAAAAAGGGG
***** *****	
14CSR	ATGTCTTTTATCTTCACGTTTAGACCAGGTGTGGCCTACCAAGTGGATCAGATTTGA
670	ATGTCTTTTATCTTCACGTTTAGACCAGGTGTGGCCTACCAAGTGGATCAGATTTGA
6BF	ATGTCTTTTATCTTCACGTTTAGACCAGGTGTGGCCTACCAAGTGGATCAGATTTGA
6BSP	ATGTCTTTTATCTTCACGTTTAGACCAGGTGTGGCCTACCAAGTGGATCAGATTTGA
19AH	ATATCTTTTATCTTCACGTTTAGATCAGGTGTGGCCTACCAAGTGGATCAGATAGTGA
23FPO	ATATCTTTTATCTTCACGTTTAGATCAGGTGTGGCCTACCAAGTGGATCAGATAGTGA
19FTW	ATATCTTTTATCTTCACGTTTAGATCAGGTGTGGCCTACCAAGTGGATCAGATAGTGA
9VSP	ATATCTTTTATCTTCACGTTTAGATCAGGTGTGGCCTACCAAGTGGATCAGATAGTGA
TIGR4	ATGTCTTTTATCTTCACGTTTAGACCAGGTGTGGCCTACCAAGTGGATCAGATTTGA
23FTW	***** *****
***** *****	
14CSR	CGGTTGAGCCAAATGACTTTGAGCCTGTCTTGATTCAACATGGGAAGATTATGCGACCT
670	CGGTTGAGCCAAATGACTTTGAGCCTGTCTTGATTCAACATGGGAAGATTATGCGACCT
6BF	CGGTTGAGCCAAATGACTTTGAGCCTGTCTTGATTCAACATGGGAAGATTATGCGACCT
6BSP	CGGTTGAGCCAAATGACTTTGAGCCTGTCTTGATTCAACATGGGAAGATTATGCGACCT
19AH	CGGTTGAGCCAAATGACTTTGAGCCTGTCTTGATTCAACATGGGAAGATTATGCGACCT
23FPO	CGGTTGAGCCAAATGACTTTGAGCCTGTCTTGATTCAACATGGGAAGATTATGCGACCT
19FTW	CGGTTGAGCCAAATGACTTTGAGCCTGTCTTGATTCAACATGGGAAGATTATGCGACCT
9VSP	CGGTTGAGCCAAATGACTTTGAGCCTGTCTTGATTCAACATGGGAAGATTATGCGACCT
TIGR4	CGGTTGAGCCAAATGACTTTGAGCCTGTCTTGATTCAACATGGGAAGATTATGCGACCT
23FTW	CGGTTGAGCCAAATGACTTTGAGCCTGTCTTGATTCAACATGGGAAGATTATGCGACCT
***** *****	
14CSR	TGTTGACCTGTACACCGTATATGATTAACAGTCATCGTCTGTTGGTACGTGGGAAGCGGA
670	TGTTGACCTGTACACCGTATATGATTAACAGTCATCGTCTGTTGGTACGTGGGAAGCGGA
6BF	TGTTGACCTGTACACCGTATATGATTAACAGTCATCGTCTGTTGGTACGTGGGAAGCGGA
6BSP	TGTTGACCTGTACACCGTATATGATTAACAGTCATCGTCTGTTGGTACGTGGGAAGCGGA
19AH	TGTTGACCTGTACACCGTATATGATTAACAGTCATCGTCTGTTGGTACGTGGGAAGCGGA
23FPO	TGTTGACTTGTACACCGTATATGATTAACAGTCATCGTCTGTTGGTACGTGGGAAGCGGA
19FTW	TACTGACTTGTACACCGTATATGATTAACAGCCACCGTTGGTACGTGGGAACACGGA
9VSP	TGTTGACTTGTACACCGTATATGATTAACAGTCATCGTCTGTTGGTACGTGGGAAGCGGA
TIGR4	TGTTGACTTGTACACCGTATATGATTAACAGTCATCGTCTGTTGGTACGTGGGAAGCGGA
23FTW	TGTTGACCTGTACACCGTATATGATTAACAGTCATCGTCTGTTGGTACGTGGGAAGCGGA
***** *****	
14CSR	TTCCGTATACGGCACCAATTGCAGAGCGAAATCGAGCGGTGAGAGAGCGTGGCAATTCT
670	TTCCGTATACGGCACCAATTGCAGAGCGAAATCGAGCGGTGAGAGAGCGTGGCAATTCT
6BF	TTCCGTATACGGCACCAATTGCAGAGCGAAATCGAGCGGTGAGAGAGCGTGGCAATTCT
6BSP	TTCCGTATACGGCACCAATTGCAGAGCGAAATCGAGCGGTGAGAGAGCGTGGCAATTCT
19AH	TTCCGTATACGGCACCAATTGCAGAGCGAAATCGAGCGGTGAGAGAGCGTGGCAATTCT
23FPO	TTCCGTATACGGCACCAATTGCAGAGCGAAATCGAGCGGTGAGAGAGCGTGGCAATTCT
19FTW	TTCCATATACAGGCCGATTGCTGAGCGGAATCGAGCGGTGAGAGAGCGTGGCAATTCT
9VSP	TTCCGTATACGGCACCAATTGCAGAGCGGAATCGAGCGGTGAGAGAGCGTGGCAATTCT
TIGR4	TTCCGTATACGGCACCAATTGCAGAGCGGAATCGAGCGGTGAGAGAGCGTGGCAATTCT
23FTW	TTCCGTATACGGCACCAATTGCAGAGCGGAATCGAGCGGTGAGAGAGCGTGGCAATTCT
***** *****	

Figure 196I

Figure 196AJ

PC T / US05 / 27239 429/487

14CSR CGCTTGGATTCGAAAATCGTATTGTAGATCCTTTGGCGAAGGGTATGAGGTAAT
 670 CGCTTGGATTCGAAAATCGTATTGTAGATCCTTTGGCGAAGGGTATGAGGTAAT
 6BF CGCTTGGATTCGAAAATCGTATTGTAGATCCTTTGGCGAAGGGTATGAGGTAAT
 6BSP CGCTTGGATTCGAAAATCGTATTGTAGATCCTTTGGCGAAGGGTATGAGGTAAT
 19AH CGCTTGGATTCGAAAATCGTATTGTAGATCCTTTGGCGAAGGGTATGAGGTAAT
 23FPO CGCTTGGCTTCGAAAATCGCATTGTAGATCCTTTGGCGAGGGATATGAGGTCAT
 19FTW CGCTTGGCTTCGAAAATCGCATTGTAGATCCTTTGGCGAGGGATATGAGGTCAT
 9VSP CGCTTGGCTTCGAAAATCGCATTGTAGATCCTTTGGCGAGGGATATGAGGTCAT
 TIGR4 CGCTTGGCTTCGAAAATCGCATTGTAGATCCTTTGGCGAGGGATATGAGGTCAT
 23FTW CGCTTGGATTGCAAATCGTATTGTAGATCCTTTGGCGAAGGGTATGAGGTAAT

14CSR TACCAAGTGTCTGACGATCCTGATGCAGTCTACGGCTATTGTCGATTCCGAGTTGGAA
 670 TACCAAGTGTCTGACGATCCTGATGCAGTCTACGGCTATTGTCGATTCCGAGTTGGAA
 6BF TACCAAGTGTCTGACGATCCTGATGCAGTCTACGGCTATTGTCGATTCCGAGTTGGAA
 6BSP TACCAAGTGTCTGACGATCCTGATGCAGTCTACGGCTATTGTCGATTCCGAGTTGGAA
 19AH TACCAAGTGTCTGACGACCCCTGATGCAGTCTATGGTTACTTGTCTATTCAAAGTTGGAA
 23FPO TACCAAGTGTCTGACGACCCCTGATGCAGTCTATGGTTACTTGTCTATTCAAAGTTGGAA
 19FTW TACCAAGTGTCTGACGACCCCTGATGCAGTCTATGGTTACTTGTCTATTCAAAGTTGGAA
 9VSP TACCAAGTGTCTGACGACCCCTGATGCAGTCTATGGTTACTTGTCTATTCAAAGTTGGAA
 TIGR4 TACCAAGTGTCTGACGATCCTGATGCAGTCTACGGCTATTGTCGATTCCGAGTTGGAA
 23FTW *****

14CSR ATCATGGAGCCAGTTATCTAGGAGCGGATTACCATCATTTAGCAATGGGGTTGGCCAT
 670 ATCATGGAGCCAGTTATCTAGGAGCGGATTACCATCATTTAGCAATGGGGTTGGCCAT
 6BF ATCATGGAGCCAGTTATCTAGGAGCGGATTACCATCATTTAGCAATGGGGTTGGCCAT
 6BSP ATCATGGAGCCAGTTATCTAGGAGCGGATTACCATCATTTAGCAATGGGGTTGGCCAT
 19AH ATCATGGAGCCAGTTATCTAGGAGCGGATTACCATCATTTAGCAATGGGGTTGGCCAT
 23FPO ATCATGGAGCCAGTTATCTAGGAGCGGATTACCATCATTTAGCAATGGGGTTGGCCAT
 19FTW ATCATGGAGCCAGTTATCTAGGAGCGGATTACCATCATTTAGCAATGGGGTTGGCCAT
 9VSP ATCATGGAGCCAGTTATCTAGGAGCGGATTACCATCATTTAGCAATGGGGTTGGCCAT
 TIGR4 ATCATGGAGCCAGTTATCTAGGAGCGGATTACCATCATTTAGCAATGGGGTTGGCCAT
 23FTW ATCATGGAGCCAGTTATCTAGGAGCGGATTACCATCATTTAGCAATGGGGTTGGCCAT

14CSR GTGGATGGACGCCTTCCTGTTGAGGAAAAGGGATTGTTCAAGTGATTGCTGGCAC
 670 GTGGATGGACGCCTTCCTGTTGAGGAAAAGGGATTGTTCAAGTGATTGCTGGCAC
 6BF GTGGATGGACGCCTTCCTGTTGAGGAAAAGGGATTGTTCAAGTGATTGCTGGCAC
 6BSP GTGGATGGACGCCTTCCTGTTGAGGAAAAGGGATTGTTCAAGTGATTGCTGGCAC
 19AH GTGGATGGTACACCGCTGCCTCTGGATGGTACAGGGATTGCTCAGTGATTGCTGGCAC
 23FPO GTGGATGGTACACCGCTGCCTCTGGATGGTACAGGGATTGCTCAGTGATTGCTGGCAC
 19FTW GTGGATGGTACACCGCTGCCTCTGGATGGTACAGGGATTGCTCAGTGATTGCTGGCAC
 9VSP GTGGATGGTACACCGCTGCCTCTGGATGGTACAGGGATTGCTCAGTGATTGCTGGCAC
 TIGR4 GTGGATGGACGCCTTCCTGTTGAGGAAAAGGGATTGTTCAAGTGATTGCTGGCAC
 23FTW *****

14CSR CGTGCAGAACCAAGCCATGTCTTTTCCGCCATTGGATCAGCTAAAAGTTGGAGATGCT
 670 CGTGCAGAACCAAGCCATGTCTTTTCCGCCATTGGATCAGCTAAAAGTTGGAGATGCT
 6BF CGTGCAGAACCAAGCCATGTCTTTTCCGCCATTGGATCAGCTAAAAGTTGGAGATGCT
 6BSP CGTGCAGAACCAAGCCATGTCTTTTCCGCCATTGGATCAGCTAAAAGTTGGAGATGCT
 19AH CGTGCAGAACCAAGCCATGTCTTTTCCGCCATTGGATCAGCTAAAAGTTGGAGATGCT
 23FPO CGTGCAGAACCAAGCCATGTCTTTTCCGCCATTGGATCAGCTAAAAGTTGGAGATGCT
 19FTW CGTGCAGAACCAAGCCATGTCTTTTCCGCCATTGGATCAGCTAAAAGTTGGAGATGCT
 9VSP CGTGCAGAACCAAGCCATGTCTTTTCCGCCATTGGATCAGCTAAAAGTTGGAGATGCT
 TIGR4 CGTGCAGAACCAAGCCATGTCTTTTCCGCCATTGGATCAGCTAAAAGTTGGAGATGCT
 23FTW *****

Figure 196AK

14CSR	CTTTATTATGATAATGCCAGGAAATTGTAGAATATCAGATGATGGACACAGAGATTATT
670	CTTTATTATGATAATGCCAGGAAATTGTAGAATATCAGATGATGGACACAGAGATTATT
6BF	CTTTATTATGATAATGCCAGGAAATTGTAGAATATCAGATGATGGACACAGAGATTATT
6BSP	CTTTATTATGATAATGCCAGGAAATTGTAGAATATCAGATGATGGACACAGAGATTATT
19AH	CTTTATTATGATAATGCCAGGAAATTGTAGAATATCAGATGATGGACACAGAGATTATT
23FPO	CTTTATTATGATAATGCCAGGAAATTGTAGAATATCAGATGATGGACACAGAGATTATT
19FTW	CTTTATTATGATAATGCCAGGAAATTGTAGAATATCAGATGATGGACACAGAGATTATT
9VSP	CTTTATTATGATAATGCCAGGAAATTGTAGAATATCAGATGATGGACACAGAGATTATT
TIGR4	CTTTATTATGATAATGCCAGGAAATTGTAGAATATCAGATGATGGACACAGAGATTATT
23FTW	CTTTATTATGATAATGCCAGGAAATTGTAGAATATCAGATGATGGACACAGAGATTATT

14CSR	TTACCGTCCAATGGAAAAATTAGAACGTTAGCTCTAAAATATCATGACCTTGATA
670	TTACCGTCCAATGGAAAAATTAGAACGTTAGCTCTAAAATATCATGACCTTGATA
6BF	TTACCGTCCAATGGAAAAATTAGAACGTTAGCTCTAAAATATCATGACCTTGATA
6BSP	TTACCGTCCAATGGAAAAATTAGAACGTTAGCTCTAAAATATCATGACCTTGATA
19AH	TTACCGTCCAATGGAAAAATTAGAACGTTAGCTCTAAAATATCATGACCTTGATA
23FPO	TTACCGTCCAATGGAAAAATTAGAACGTTAGCTCTAAAATATCATGACCTTGATA
19FTW	TTACCGTCCAATGGAAAAATTAGAACGTTAGCTCTAAAATATCATGACCTTGATA
9VSP	TTACCGTCCAATGGAAAAATTAGAACGTTAGCTCTAAAATATCATGACCTTGATA
TIGR4	TTACCGTCCAATGGAAAAATTAGAACGTTAGCTCTAAAATATCATGACCTTGATA
23FTW	TTACCGTCCAATGGAAAAATTAGAACGTTAGCTCTAAAATATCATGACCTTGATA

14CSR	ACCTGCGATCCGATTCTACCTTTAATAAACGCTTATTAGTGAATTTCGAGTCGCT
670	ACCTGCGATCCGATTCTACCTTTAATAAACGCTTATTAGTGAATTTCGAGTCGCT
6BF	ACCTGCGATCCGATTCTACCTTTAATAAACGCTTATTAGTGAATTTCGAGTCGCT
6BSP	ACCTGCGATCCGATTCTACCTTTAATAAACGCTTATTAGTGAATTTCGAGTCGCT
19AH	ACCTGCGATCCGATTCTACCTTTAATAAACGCTTATTAGTGAATTTCGAGTCGCT
23FPO	ACCTGCGATCCGATTCTACCTTTAATAAACGCTTATTAGTGAATTTCGAGTCGCT
19FTW	ACCTGCGATCCGATTCTACCTTTAATAAACGCTTATTAGTGAATTTCGAGTCGCT
9VSP	ACCTGCGATCCGATTCTACCTTTAATAAACGCTTATTAGTGAATTTCGAGTCGCT
TIGR4	ACCTGCGATCCGATTCTACCTTTAATAAACGCTTATTAGTGAATTTCGAGTCGCT
23FTW	ACCTGCGATCCGATTCTACCTTTAATAAACGCTTATTAGTGAATTTCGAGTCGCT

14CSR	GTTTATCAAAATCAGATCCACAAACAGCTGCAGTTGCGAGGGTTGCTTTACGAAAGAA
670	GTTTATCAAAATCAGATCCACAAACAGCTGCAGTTGCGAGGGTTGCTTTACGAAAGAA
6BF	GTTTATCAAAATCAGATCCACAAACAGCTGCAGTTGCGAGGGTTGCTTTACGAAAGAA
6BSP	GTTTATCAAAATCAGATCCACAAACAGCTGCAGTTGCGAGGGTTGCTTTACGAAAGAA
19AH	GTTTATCAAAATCAGATCCACAAACAGCTGCAGTTGCGAGGGTTGCTTTACGAAAGAA
23FPO	GTTTATCAAAATCAGATCCACAAACAGCTGCAGTTGCGAGGGTTGCTTTACGAAAGAA
19FTW	GTTTATCAAAATCAGATCCACAAACAGCTGCAGTTGCGAGGGTTGCTTTACGAAAGAA
9VSP	GTTTATCAAAATCAGATCCACAAACAGCTGCAGTTGCGAGGGTTGCTTTACGAAAGAA
TIGR4	GTTTATCAAAATCAGATCCACAAACAGCTGCAGTTGCGAGGGTTGCTTTACGAAAGAA
23FTW	GTTTATCAAAATCAGATCCACAAACAGCTGCAGTTGCGAGGGTTGCTTTACGAAAGAA

14CSR	GGACAATCTGTATCGCGTGTGCAACCTCTCAATGGTTGTAACCGTGGCTAGTGGTACTG
670	GGACAATCTGTATCGCGTGTGCAACCTCTCAATGGTTGTAACCGTGGCTAGTGGTACTG
6BF	GGACAATCTGTATCGCGTGTGCAACCTCTCAATGGTTGTAACCGTGGCTAGTGGTACTG
6BSP	GGACAATCTGTATCGCGTGTGCAACCTCTCAATGGTTGTAACCGTGGCTAGTGGTACTG
19AH	GGACAATCTGTATCGCGTGTGCAACCTCTCAATGGTTGTAACCGTGGCTAGTGGTACTG
23FPO	GGACAATCTGTATCGCGTGTGCAACCTCTCAATGGTTGTAACCGTGGCTAGTGGTACTG
19FTW	GGACAATCTGTATCGCGTGTGCAACCTCTCAATGGTTGTAACCGTGGCTAGTGGTACTG
9VSP	GGACAATCTGTATCGCGTGTGCAACCTCTCAATGGTTGTAACCGTGGCTAGTGGTACTG
TIGR4	GGACAATCTGTATCGCGTGTGCAACCTCTCAATGGTTGTAACCGTGGCTAGTGGTACTG
23FTW	GGACAATCTGTATCGCGTGTGCAACCTCTCAATGGTTGTAACCGTGGCTAGTGGTACTG

Figure 196AL

PCT/US05/23392 431/487

14CSR	GCATTTCTGGGAATCCTGTTGTTTGTGGAAGCTAGCACGTTACTACGAGGGAAATAA
670	GCATTTCTGGGAATCCTGTTGTTTGTGGAAGCTAGCACGTTACTACGAGGGAAATAA
6BF	GCATTTCTGGGAATCCTGTTGTTTGTGGAAGCTAGCACGTTACTACGAGGGAAATAA
6BSP	GCATTTCTGGGAATCCTGTTGTTTGTGGAAGCTAGCACGTTACTACGAGGGAAATAA
19AH	GCATTTATGGGAATCCTGTTGTTTGTGGAAGCTAGCACGTTACTACGAGGGAAATAA
23FPO	GCATTTCTGGGAATCCTGTTGTTTGTGGAAGCTAGCACGTTACTACGAGGGAAATAA
19FTW	GCATTTCTGGGAATCCTGTTGTTTGTGGAAGCTAGCACGTTACTACGAGGGAAATAA
9VSP	GCATTTCTGGGAATCCTGTTGTTTGTGGAAGCTAGCACGTTACTACGAGGGAAATAA
TIGR4	GCATTTCTGGGAATCCTGTTGTTTGTGGAAGCTAGCACGTTACTACGAGGGAAATAA
23FTW	GCATTTCTGGGAATCCTGTTGTTTGTGGAAGCTAGCACGTTACTACGAGGGAAATAA

14CSR	AAAGAAATGAAAGGAAAGCTAACGGCTGTTCCCTTTCCGGCTCTTGTCAACTGTAGGGG
670	AAAGAAATGAAAGGAAAGCTAACGGCTGTTCCCTTTCCGGCTCTTGTCAACTGTAGGG
6BF	AAAGAAATGAAAGGAAAGCTAACGGCTGTTCCCTTTCCGGCTCTTGTCAACTGTAGGG
6BSP	AAAGAAATGAAAGGAAAGCTAACGGCTGTTCCCTTTCCGGCTCTTGTCAACTGTAGGG
19AH	AAAGAAATGAAAGGAAAGCTAACGGCTGTTCCCTTTCCGGCTCTTGTCAACTGTAGGG
23FPO	AAAGAAATGAAAGGAAAGCTAACGGCTGTTCCCTTTCCGGCTCTTGTCAACTGTAGGG
19FTW	AAAGAAATGAAAGGAAAGCTAACGGCTGTTCCCTTTCCGGCTCTTGTCAACTGTAGGG
9VSP	AAAGAAATGAAAGGAAAGCTAACGGCTGTTCCCTTTCCGGCTCTTGTCAACTGTAGGG
TIGR4	AAAGAAATGAAAGGAAAGCTAACGGCTGTTCCCTTTCCGGCTCTTGTCAACTGTAGGG
23FTW	AAAGAAATGAAAGGAAAGCTAACGGCTGTTCCCTTTCCGGCTCTTGTCAACTGTAGGG

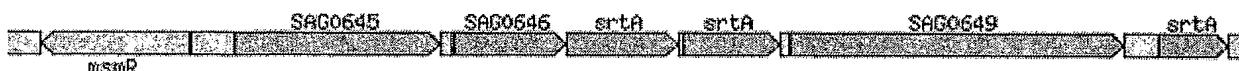
Figure 196AM

Figure 197

A

GBS80 GBS52

GBS104



B

Intergenic region between AraC R and GBS 80**AraC..CAT**

TTGATAGACCGC**TTTC**ATTATCATTCTAGAATTTCCTTAGGTTGTA
 AAGACTACAAAATAAAATGATGAAAACA**ACTATCTTG**TGGATA**CACTAAA**
 AAGACACG**CTAATT**AGCAA**ACTCTCT**CATCAT**CTCACC**ATTATTA
 TACTAC**TATTTATAT**GACAAATAAGGT**GATT****TGTTAAA**ATATAACTTT
 GAAAATCCACATATATTTAATCTTCCGTCTG**AAAAAA**TAATAAAAAAT
 AGTAAAATAAACACGAATTAAAATAAGCAA**ATTTAAGAAA**ATCTG
 TGCTAA**ACTTTAATAGTTTG**GCTTAATAATAATCAGCACTACAAAGA
 ACAAAGGGAAAAGCGA**GGAGAGA**ACTTTA **ATG.. GBS80**

C

187	4A		5A		5A
233	6A		6A		7A
Strain	FACS a -80	Strain	FACS a -80	Strain	FACS a -80
1998	95	5364	454	2129	57
2110	0	JMV071	556	2274	113
2603	62	JM91003	587	5401	170
3050	43	CJB111	365	5408	0
5376	165			5518	31
M781	65			CJB110	71
COH1	305 (G->T 179)			J7357B	91
18rs 21	0 (STOP, no LPXTG)			COH31	0

PCT/US2005/027239
433/487

AI-1									
		aa	M1	M3	M5	M18	M49	M6	M12
M6									
50913503	M6_Spy0157	LPXTG	628	gas15 30%in593aa	M3-0098 46%in256aa M3-0104 28%in563aa	M18-0132 24%in701aa	M12-4134 74%in703aa	Fibronecti n-binding protein (protein F)	
50913505	M6_Spy0159	LPXSG	1037	M3-0104 25%in339aa			M12-4141 37%in98aa	Collagen adhesion protein	
50913506	M6_Spy0160	LPXTG	557					Fimbrial structural subunit	

Figure 198

AI-2						
M1		aa	M1	M3	M5	M18
gas15	gas15	WVXTG	762	M3-0098 50%in738aa	M5-orf78 60%in462aa	M18-0126 54%in469aa
3621428	SPy0128 gas16	EVXTG	340	M3-0100 40%in354aa	M5-orf80 41%in358aa	M18-0128 38%in357aa
13621430	SPy0130 gas18	LPXTG	215	M3-0102 32%200aa	M5-orf82 31%in213aa	M18-0130 32%in213aa
						M12-4139 31%in206aa
						hypothetic al protein (fimbria)

Figure 199

AI-3									
M3		aa	M1	M3	M5	M18	M49	M6	M12
21909634	SpyM3_0098	VPXTG	744	gas15 51%in739aa	M5-off78 58%in484aa	M18-0126 74%in482aa		M12-4135 55%in751aa	putative collagen binding protein (Cpb)
21909636	SpyM3_0100	QVXTG	344	gas16 40%in354aa	M5-off80 64%in349aa	M18-0128 67%in345aa		M12-4137 61%in344aa	conserved hypothetic al protein (fimbrial)
21909638	SpyM3_0102	LPXAG	195	gas18 32%in200aa	M5-off82 98%in183aa	M18-0130 97%in183aa		M12-4139 99%in183aa	hypothetic al protein
21909640	SpyM3_0104	LPXTG	696		M5-off84 88%in656aa	M18-0132 88%in656aa		M12-4141 59%in612aa	protein F2 like fibronectin -binding

Figure 200A

M18									
19745301	spyM18_0126	VPXTG	524	gas15 54%in469aa	M3-0098 74%in482	M5-orf78 61%in528aa		M12-4135 59%in489aa	putative collagen binding protein (Cpb)
19745303	spyM18_0128	QVXTG	344	gas16 38%in357aa	M3-0100 67%in345aa	M5-orf80 60%in349aa		M12-4137 62%in344aa	conserved hypothetic al protein (fimbrial)
19745305	spyM18_0130	LPXAG	195	gas18 32%in213aa	M3-0102 97%in189aa	M5-orf82 99%in195aa		M12-4139 97%in189aa	hypothetic al protein
19745307	spyM18_0132	LPXTG	696		M3-0104 88%in656aa	M5-orf84 100%in696aa		M12-4141 50%in701aa	protein F2 like fibronectin -binding

Figure 200B

PCT/US05/27239
437/487

M5								
orf78	VPXTG	523	gas15 60%in462aa	M3-0098 58%in481aa		M18-0126 61%in528aa		M12-4135 80%in484aa
orf80	QVXTG	352	gas16 39%in356aa	M3-0100 64%in349aa		M18-0128 60%in349aa		M12-4137 65%in348aa
								conserved hypothetic al protein (fimbrial)
orf82	LPXAG	224	gas18 31%in213aa	M3-0102 98%in183aa		M18-0130 99%in195aa		M12-4139 98%in189aa
orf84	LPXTG	696		M3-104 88%in656aa		M18-0132 100%in696aa		M12-4141 50%in701aa
								protein F2 like fibronectin -binding

Figure 200C

M49								
56808848	VPXTG	744	gas15 55%in738aa	M3-0098 72%in743aa	M5-orf78 78%in483	M18-0126 61% in484	M12-4135 73%in752aa	putative collagen binding protein (Cpb)
56808846	QVXTG	344	gas16 36%in355aa	M3-0100 66%in345aa	M5-orf80 61%in349aa	M18-0128 90%in344aa	M12-4137 62%in344aa	conserved hypothetic al protein (Imbria)
56808844	LPXAG	189	gas18 31%in206aa	M3-102 98%in189aa	M5-orf82 98%in189aa	M18-0130 98%in189aa	M12-4139 98%in189aa	hypothetic al protein
56808842	LPXTG	1160		M3-104 59%in612aa	M5-orf84 50%in701aa	M18-0132 50%in701aa	M6-0157 32%in296aa	protein F2 like fibronectin -binding

Figure 200D

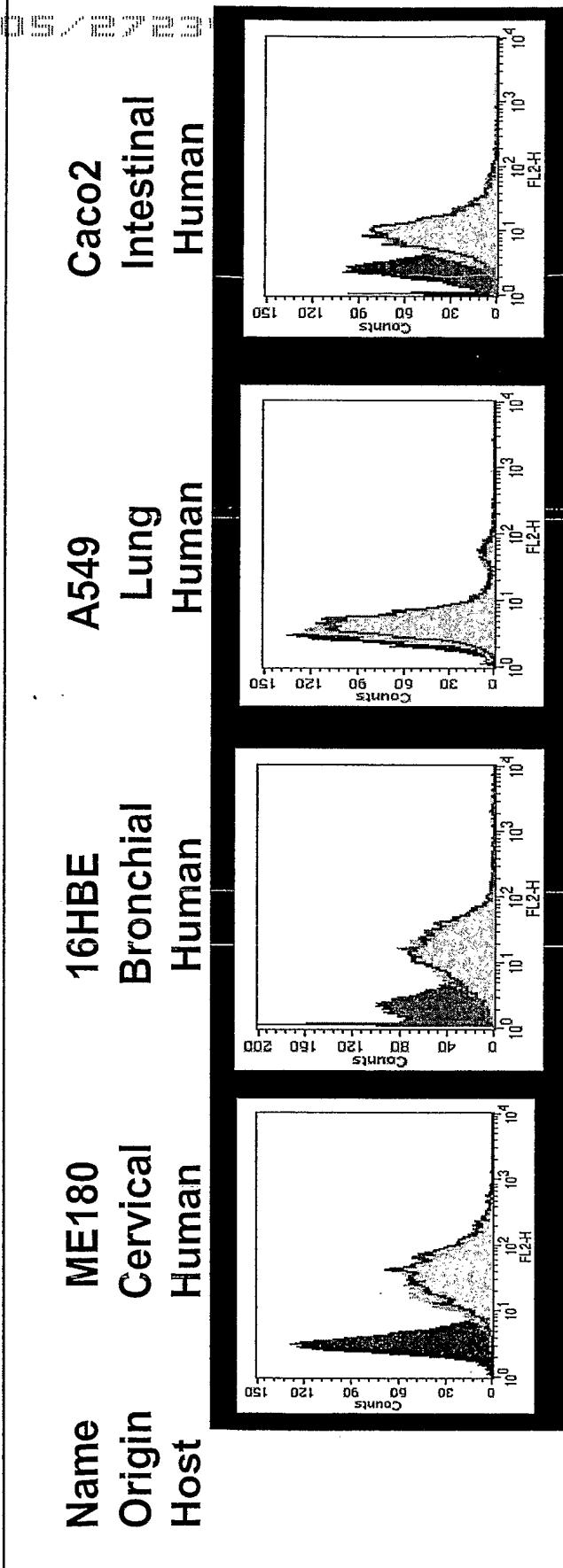
AI-4							
M12		aa	M1	M3	M5	M18	M49 M6 M12
19224134	LPXTG	698	gas15 44%in297aa	M3-0098 49%in254aa			M6-0157 74%in703aa protein F
19224135	VPXTG	756	gas15 54%in747aa	M3-0098 55%in751aa	orf78 80%in484aa	M18-0126 59%in483aa	M6-0157 51%in275aa Cpa
19224137	QVXTG	342	gas16 40%in354aa	M3-0100 61%in344aa	orf80 65%in384aa	M18-0128 62%in344aa	Ets SLA (Imperial)
19224139	LPXAG	189	gas18 31%in206aa	M3-0102 99%in183aa	orf82 98%in189aa	M18-130 97%in189aa	Orf2
19224141	LPXTG	1161		M3-0104 59%in612aa	orf84 50%in701aa	M18-0132 50%in701aa	protein F2

Figure 201

Figure 202

3S80 recombinant protein does not bind to epithelial cells

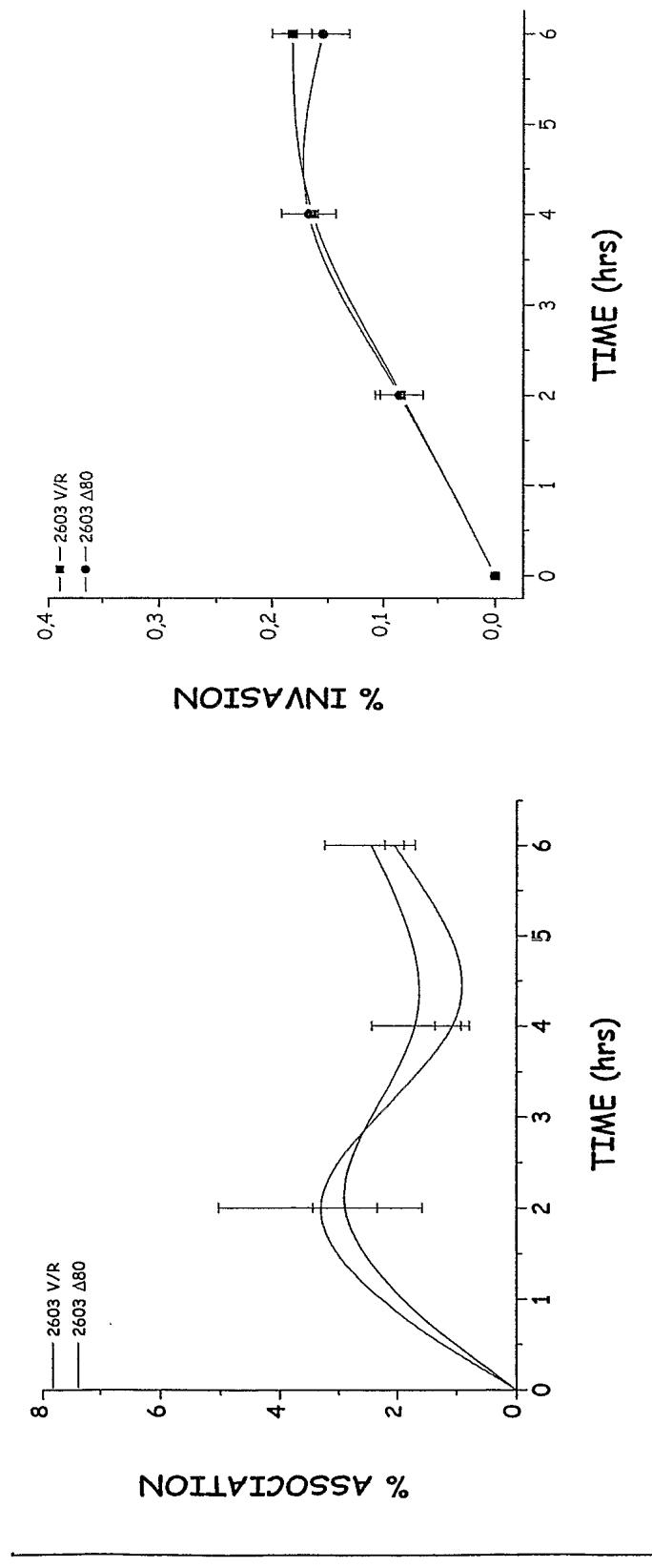
WO 2006/078318
PCT/US2005/027239



Epithelial cells were incubated in the presence or absence of GBS80 protein and then a mouse a-GBS80 polyclonal antibody added. The cell were then stained with FITC-conjugated a-mouse IgG antibody. The violet area indicates cells treated with FITC-conjugated antibody alone. GBS80 binding, expressed as Dmean channel values, was measured by FACScan cytometer as difference in fluorescence intensity between cell incubated with or without GBS80. The same protocol was used for GRQ101 protein binding to epithelial cells.

Figure 203

Deletion of GBS80 protein does not affect the ability of GBS to adhere and invade ME180



ME180 cervical carcinoma epithelial cells were infected with GBS 2603 wild type or 2603 D80 isogenic mutant. After 2h infection, non-adherent bacteria were washed off and infection prolonged for further 2h and 4h. In invasion experiments, after each time point followed a 2h antibiotic treatment. Cells were then lysed with 1% saponin and lysates plated on TSA plates.

Figure 204

GBS80 binds to ECM proteins

ELISA with purified ECM components and native GBS80 protein

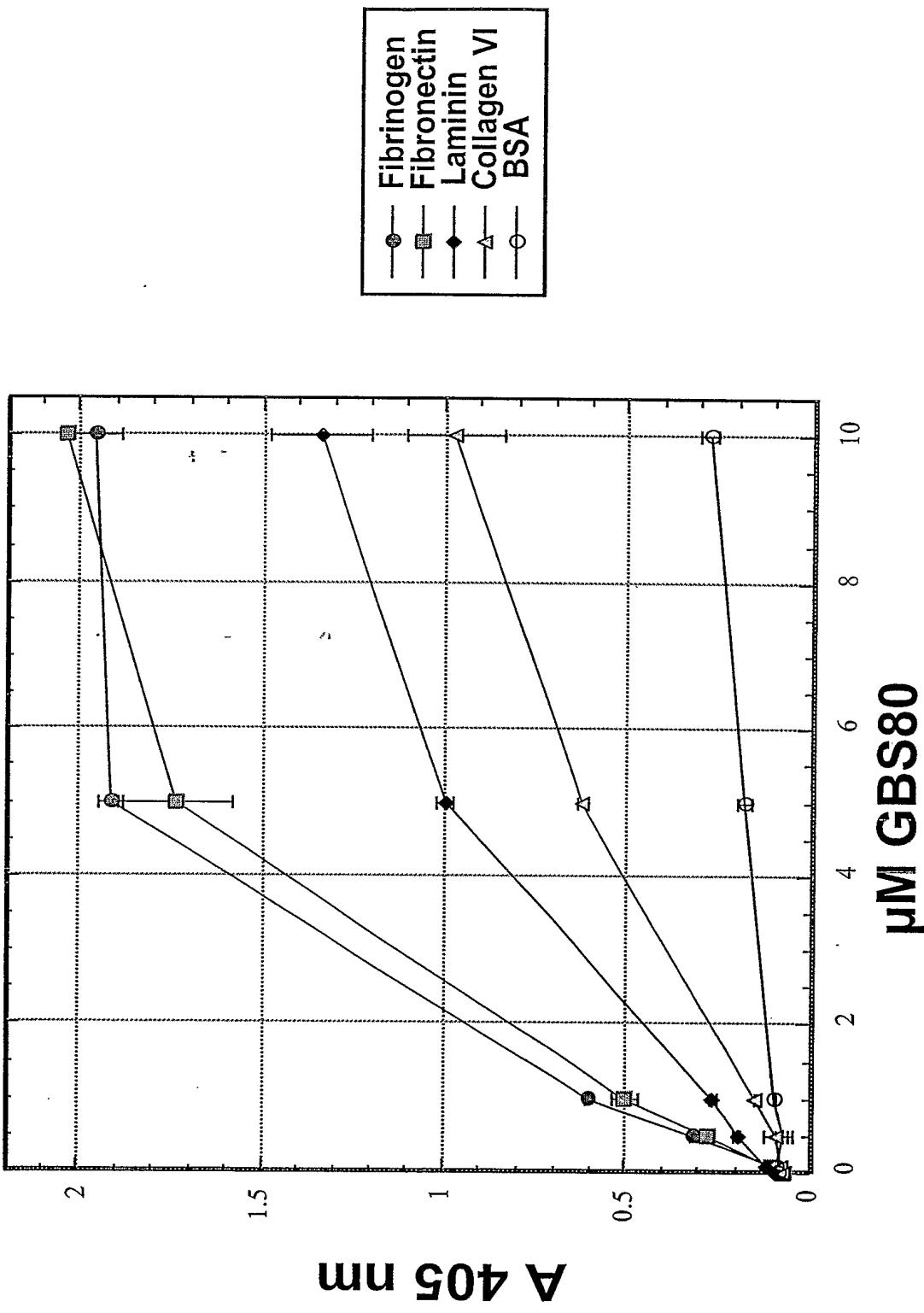
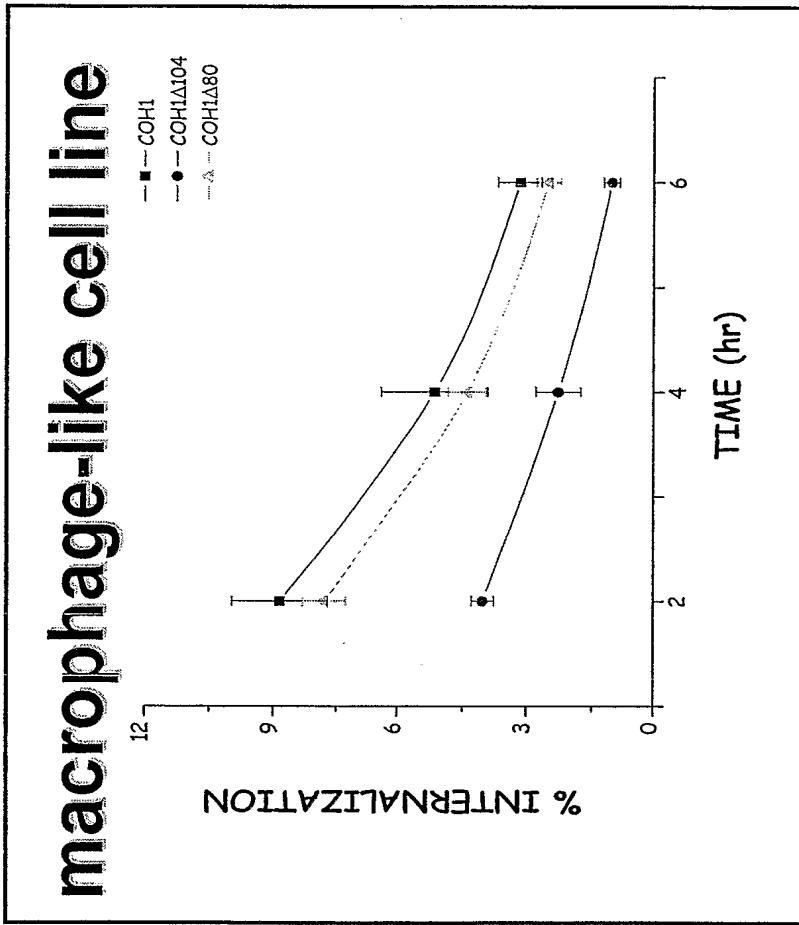


Figure 205

Deletion of GBS104 protein, but not GBS80, reduces the capacity of GBS to invade J774



J774 cells were infected with GBS COH1 wild type or COH1 Δ GBS104/COH1 Δ GBS80 isogenic mutants. After 1h infection, non-adherent bacteria were washed off and intracellular bacteria recovered at 2h, 4h and 6h post-antibiotic treatment. At each time point cells were lysed with 0.25% Triton X-100 and

Figure 206

GBS104 knockout mutant strain translocates through an epithelial monolayer less efficiently than the isogenic wild type

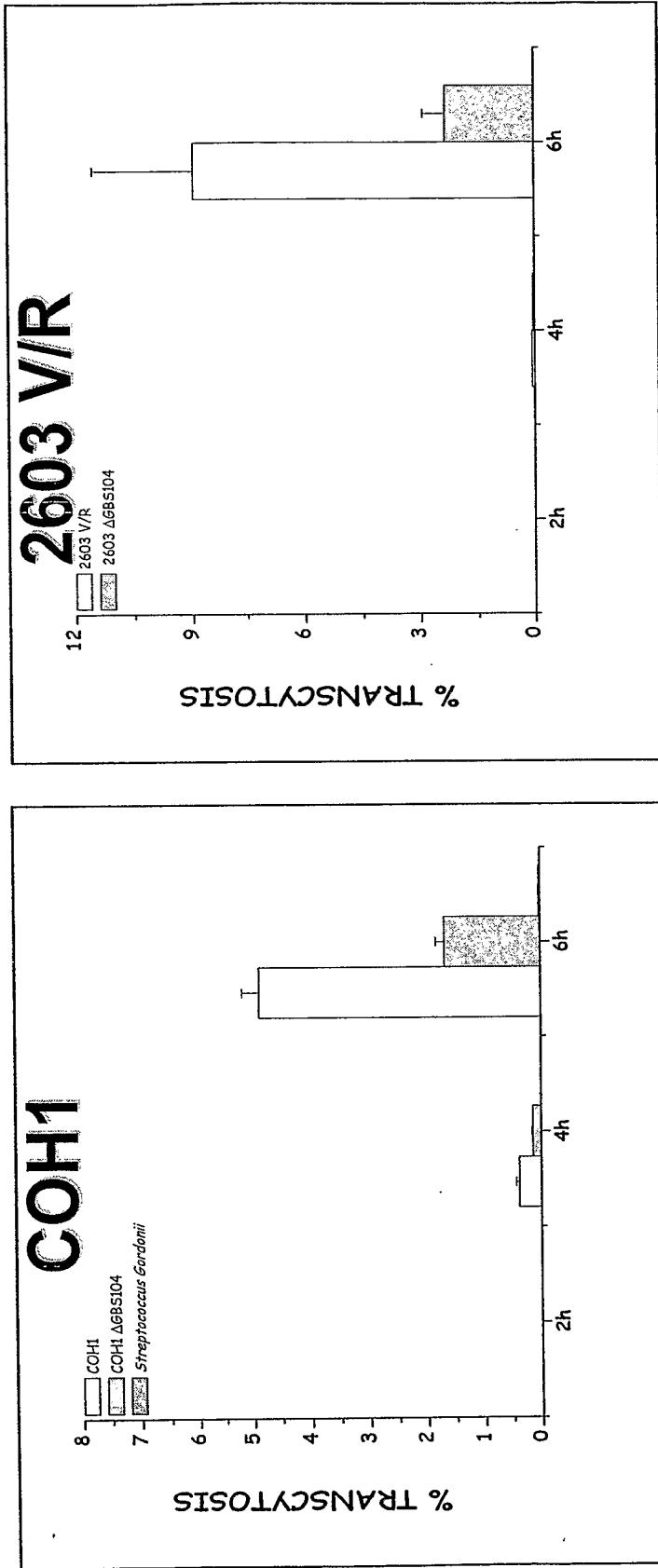


Figure 207

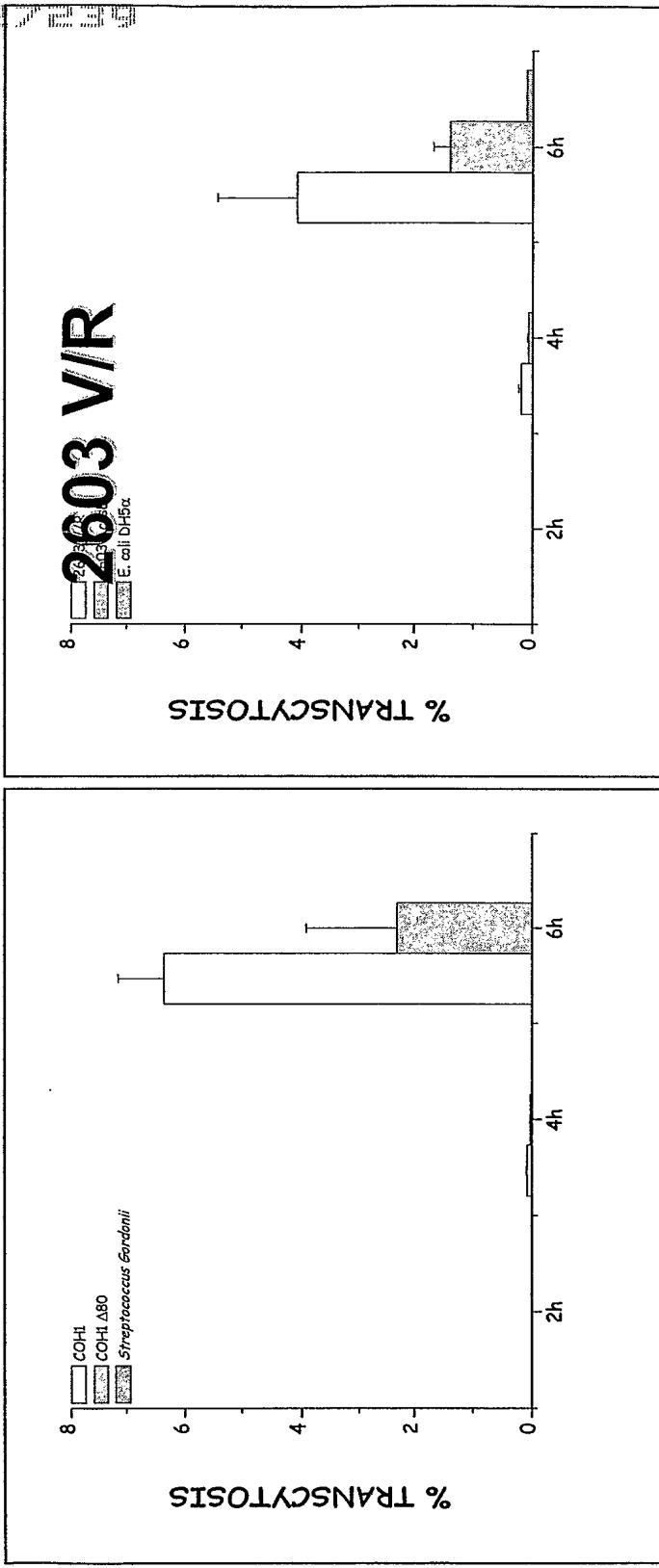
GBS80 knockout mutant strain partially loses the ability to translocate through an epithelial monolayer

WO 2006/078318

445/487

PCT/US2005/027239

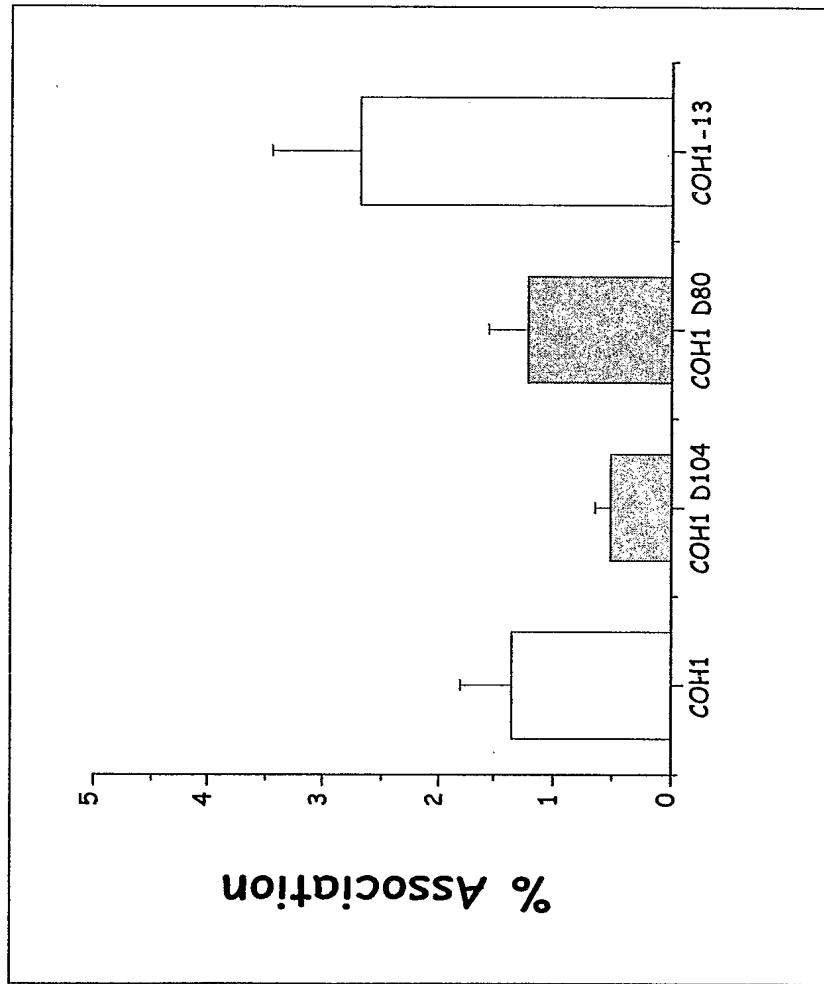
PCT/US05/E7239



Epithelial cells monolayers were inoculated with each bacterium in the apical chamber of a transwell system for 2h and then non-adherent bacteria washed off. Infection was prolonged for further 2h and 4h. Samples were taken from the media of the basolateral side and the number of colony forming units measured. Transepithelial electrical resistance measured prior and after infection gave comparable values, indicating the maintenance of the integrity of the monolayer.

Figure 208

GBS adherence to HUVEC endothelial cells



HUVEC cells were infected with GBS COH1 wild type or COH1DGBS104/COH1DGBS80 isogenic mutants. After 1h infection, non-adherent bacteria were washed off and cells lysed with 1% saponin and lysates plated on TSA plates.

Figure 209

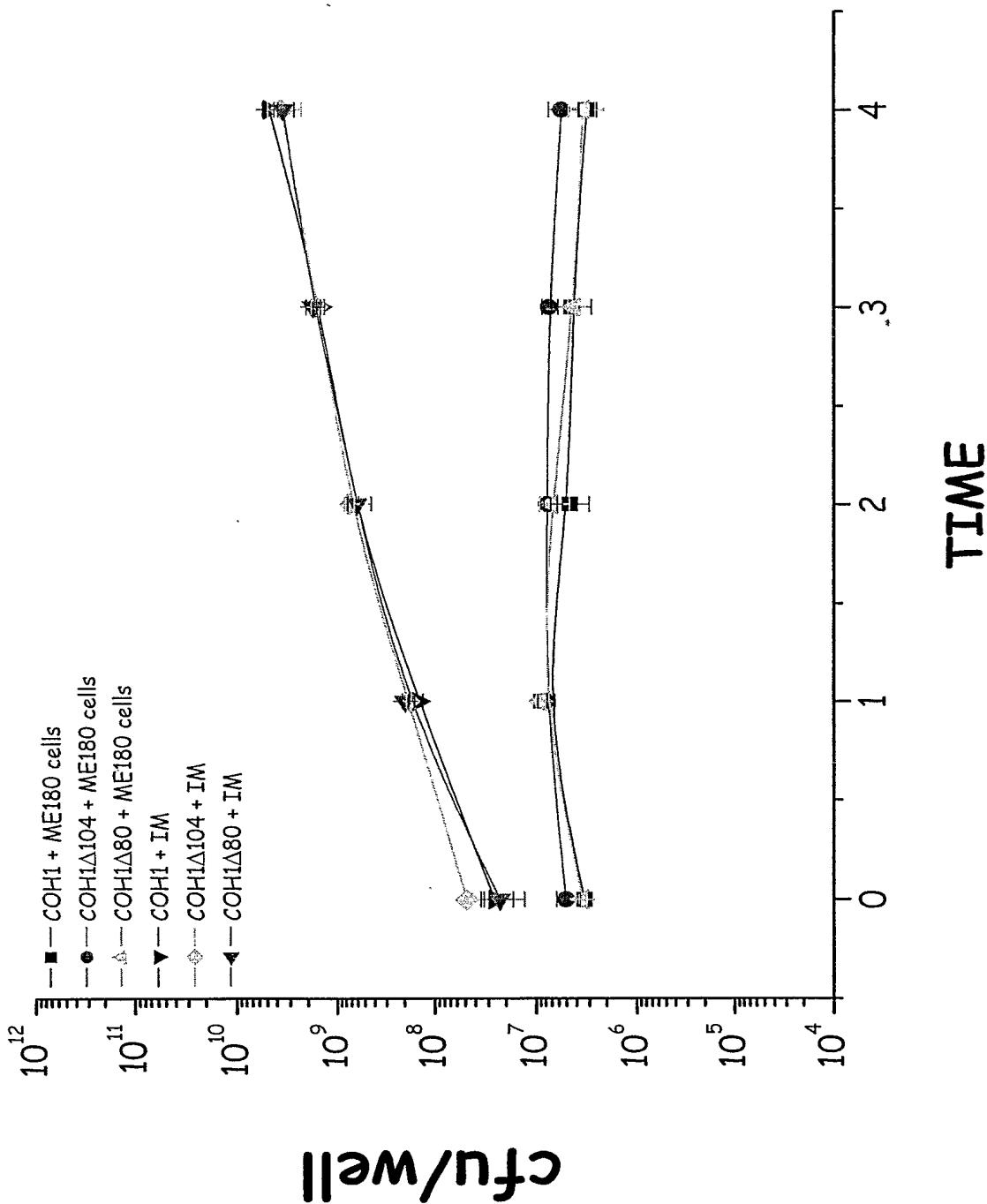


Figure 210

Binding of recombinant GBS104 protein to epithelial ce

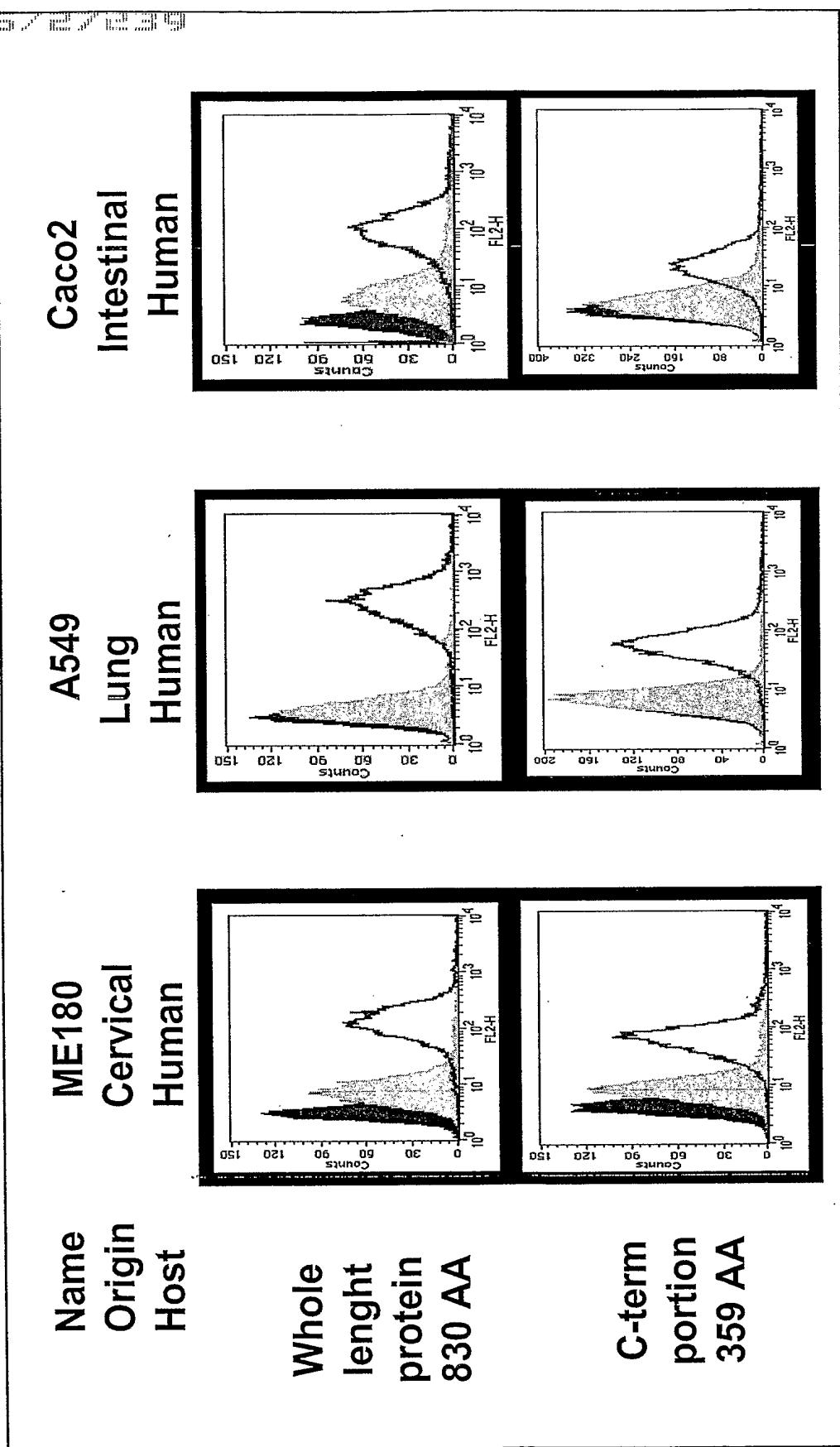
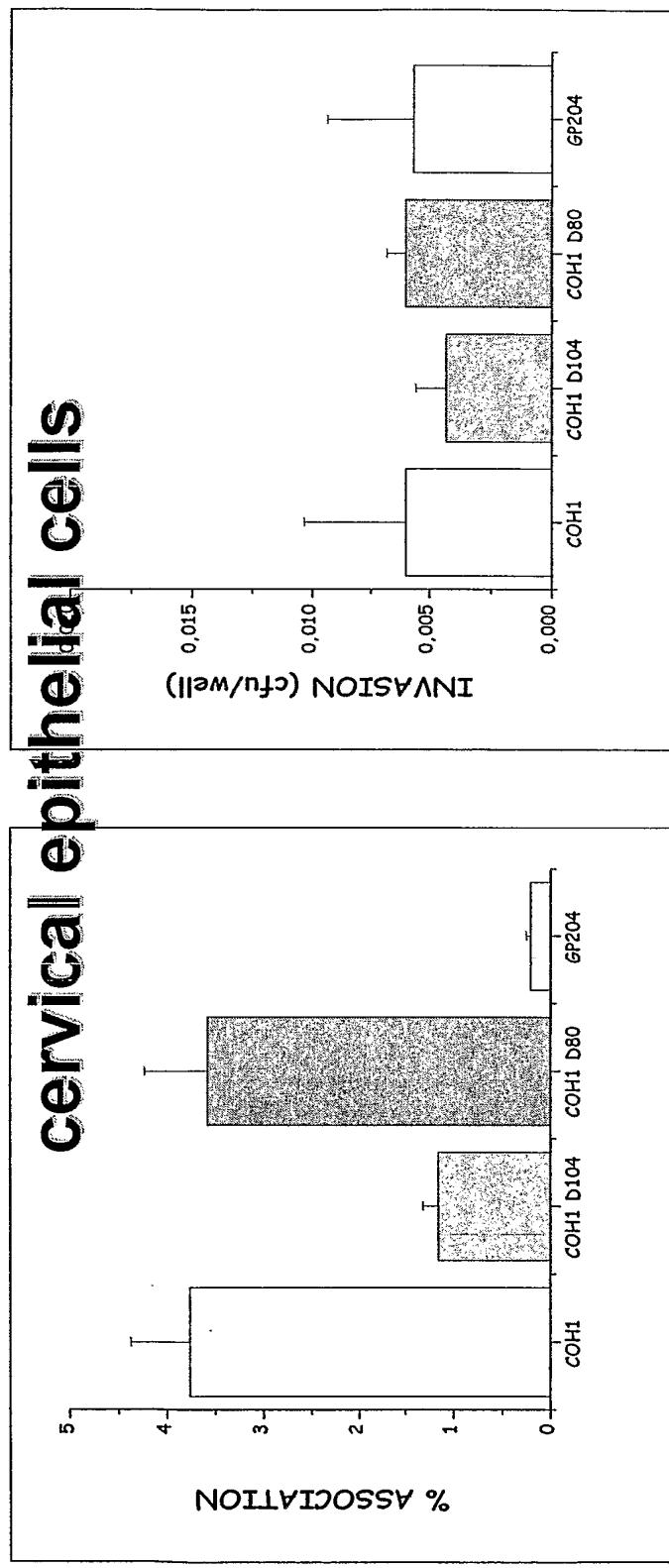


Figure 211

Deletion of GBS104 protein in the GBS strain COH1 reduces the ability of GBS to adhere to ME180



ME180 cervical carcinoma epithelial cells were infected with GBS COH1 wild type or COH1DGBS104/ COH1DGBS80 isogenic mutants. After 1h infection, non-adherent bacteria were washed off and cells lysed with 1% saponin and lysates plated on TSA plates

Figure 212

**COH1 overexpressing GBS80 protein has
an impaired capacity to translocate
through an epithelial monolayer**

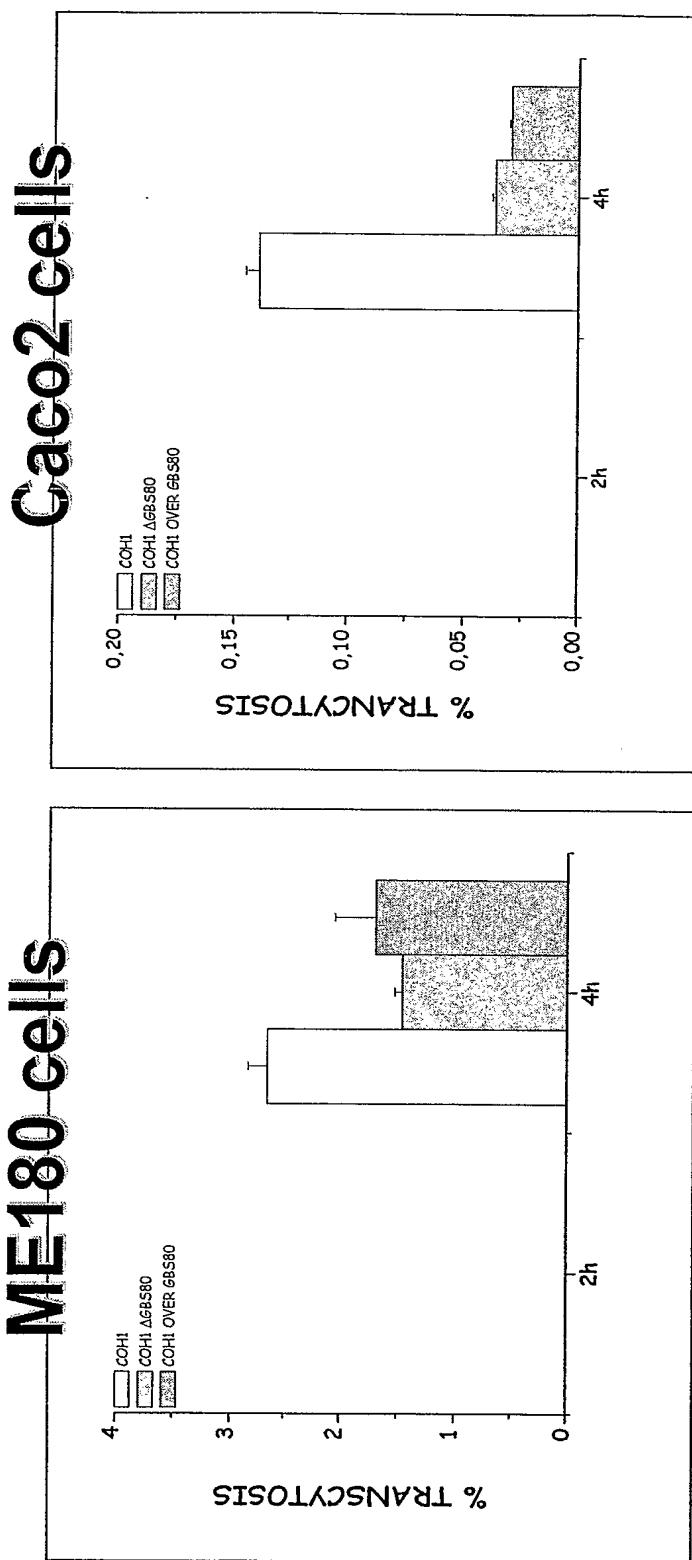
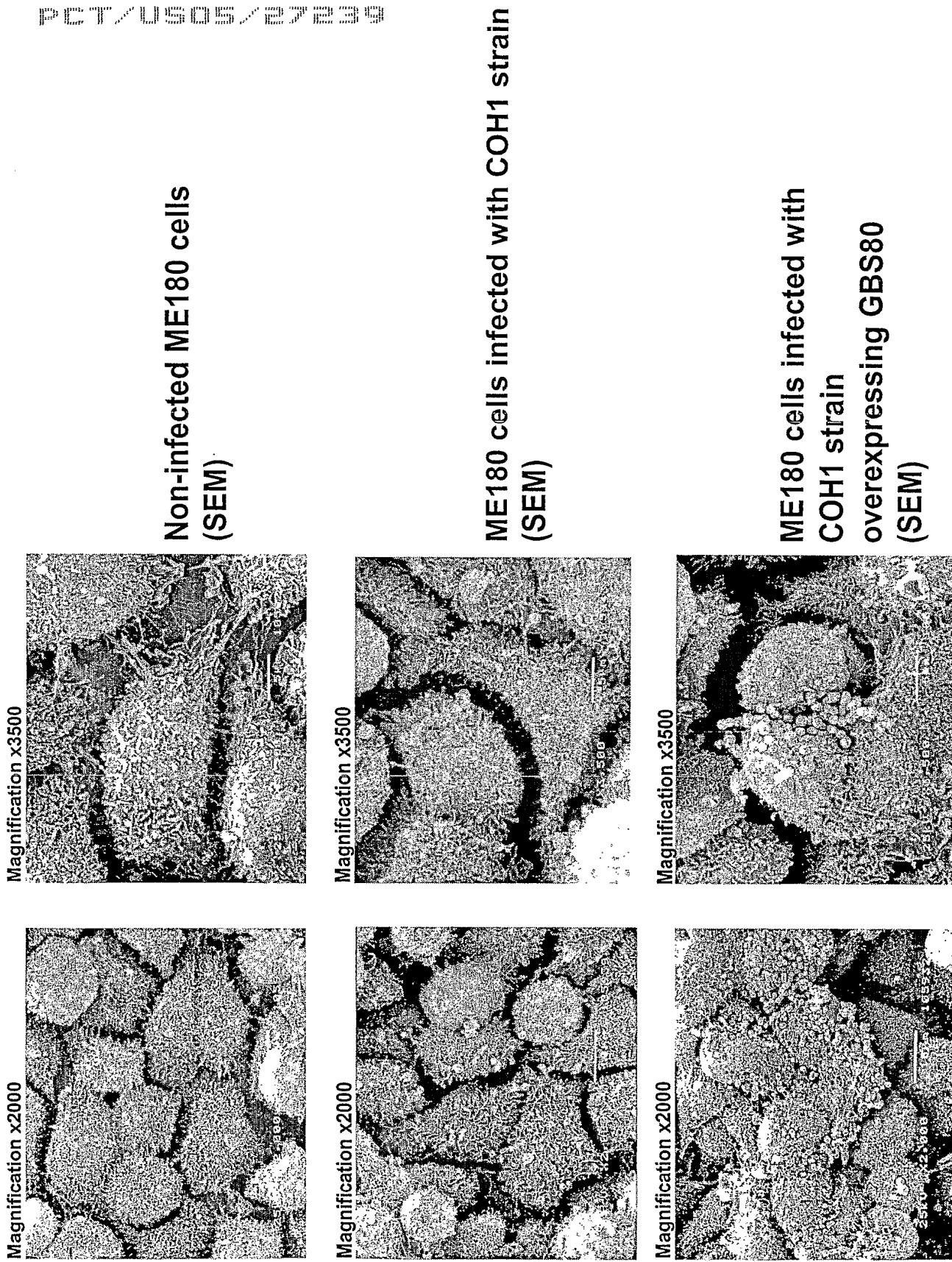


Figure 213



452/487

WO 2006/078318

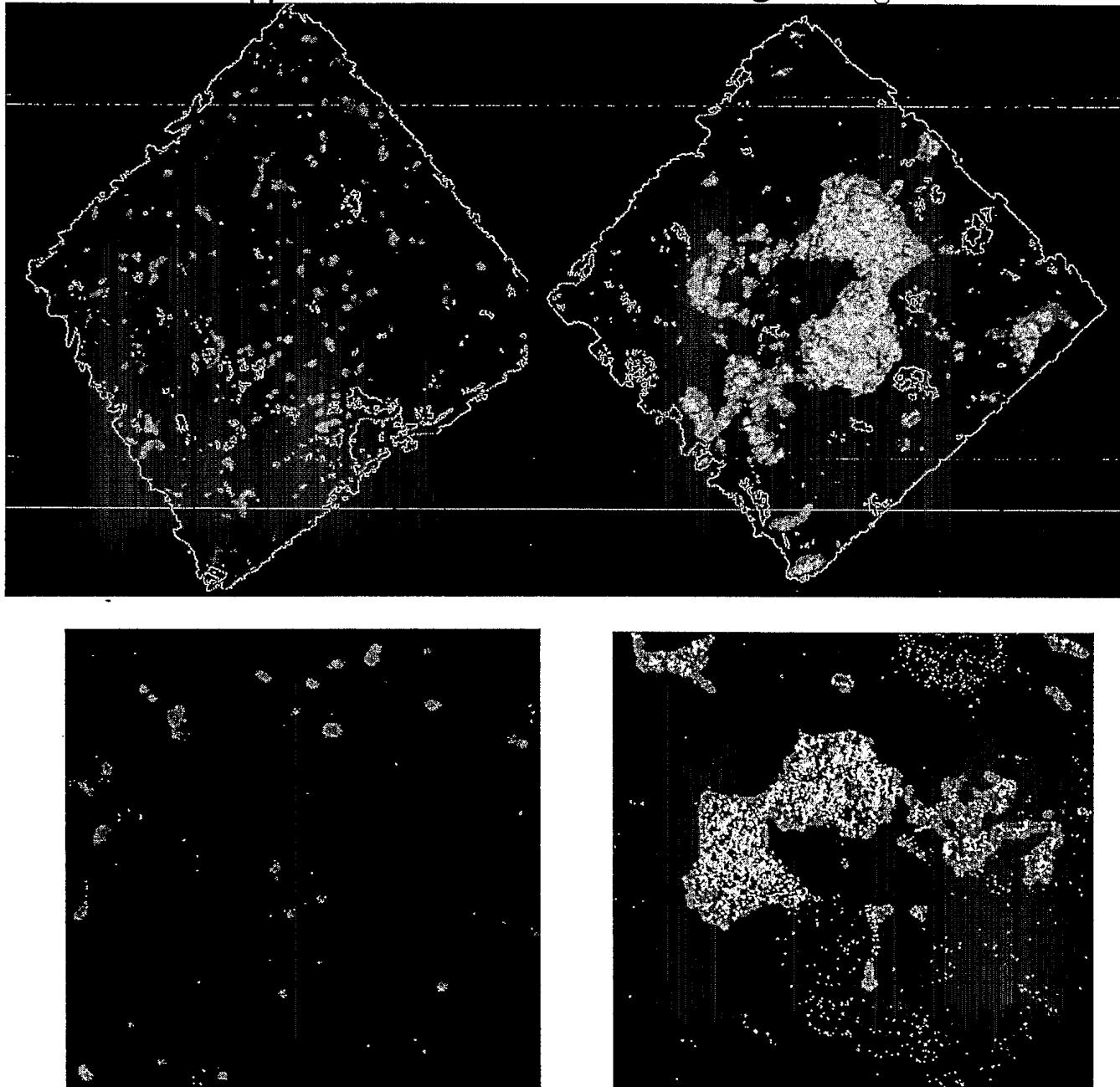
PCT/US2005/027239

PCT/US2005/027239

Figure 214

DH1 infection of ME180 cells
F-actin Blue
 α - serotype III capsule Red
 α -GBS80 Green

OH1 overexpressing GBS80
infection of ME180 cells
F-actin Blue
 α - serotype III capsule Red
 α -GBS80 Green



WO 2006/078318
PCT/US2005/027239

453/487

PCT/US2005/027239

515 △59 WT

α59

Figure 215

515 WT

α59

454/487

WO 2006/078318

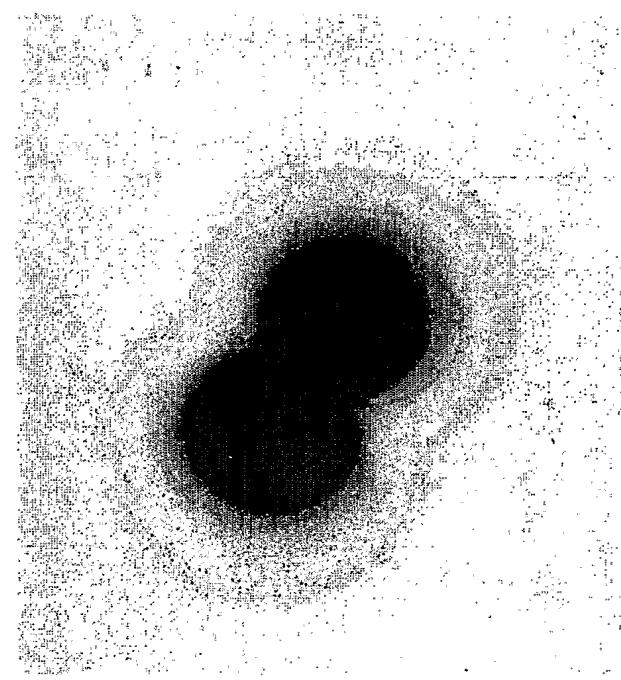
PCT/US2005/027239

PCT/US2005/027239

Figure 216

515 WT

515 △67p67



α67

515 △67

α67

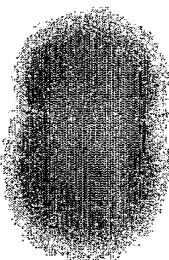


Figure 217

GBS 67 binds to fibronectin

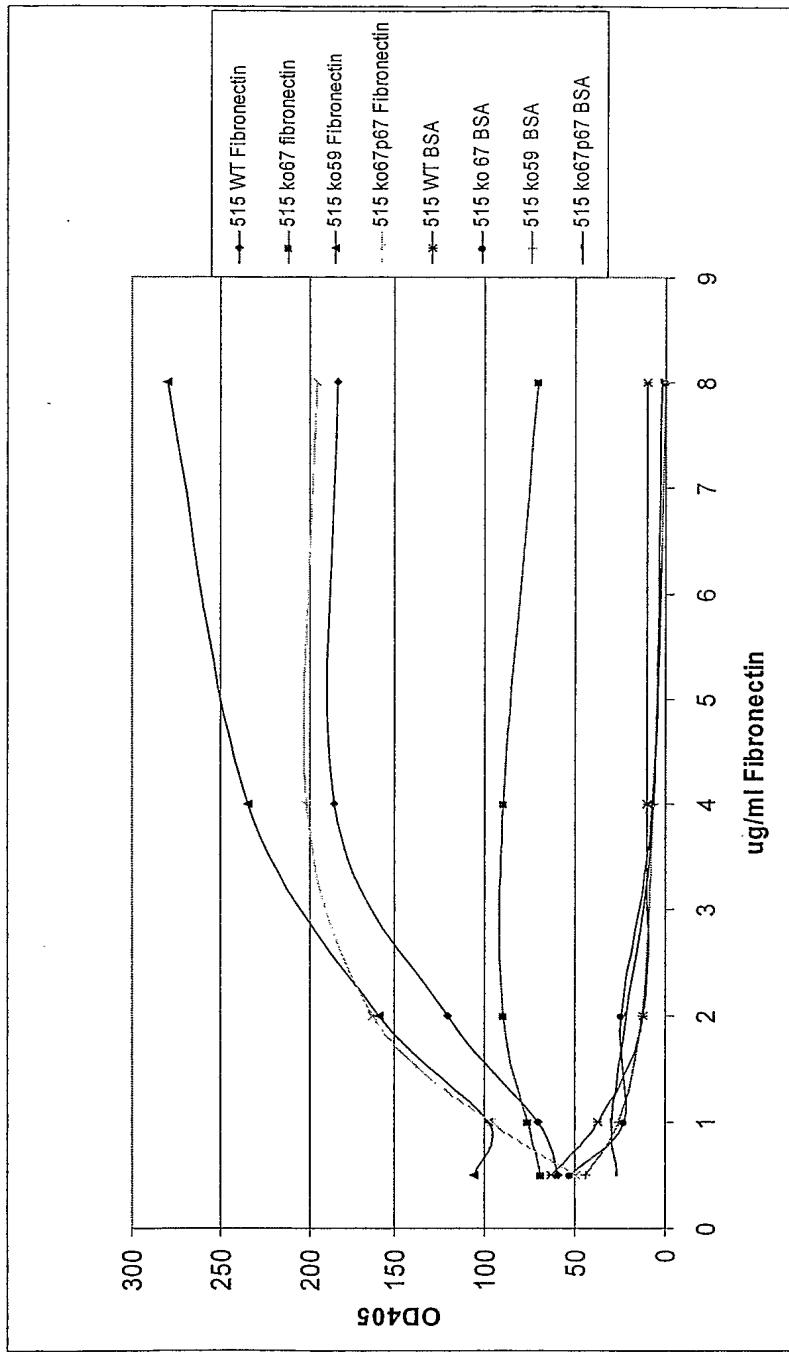


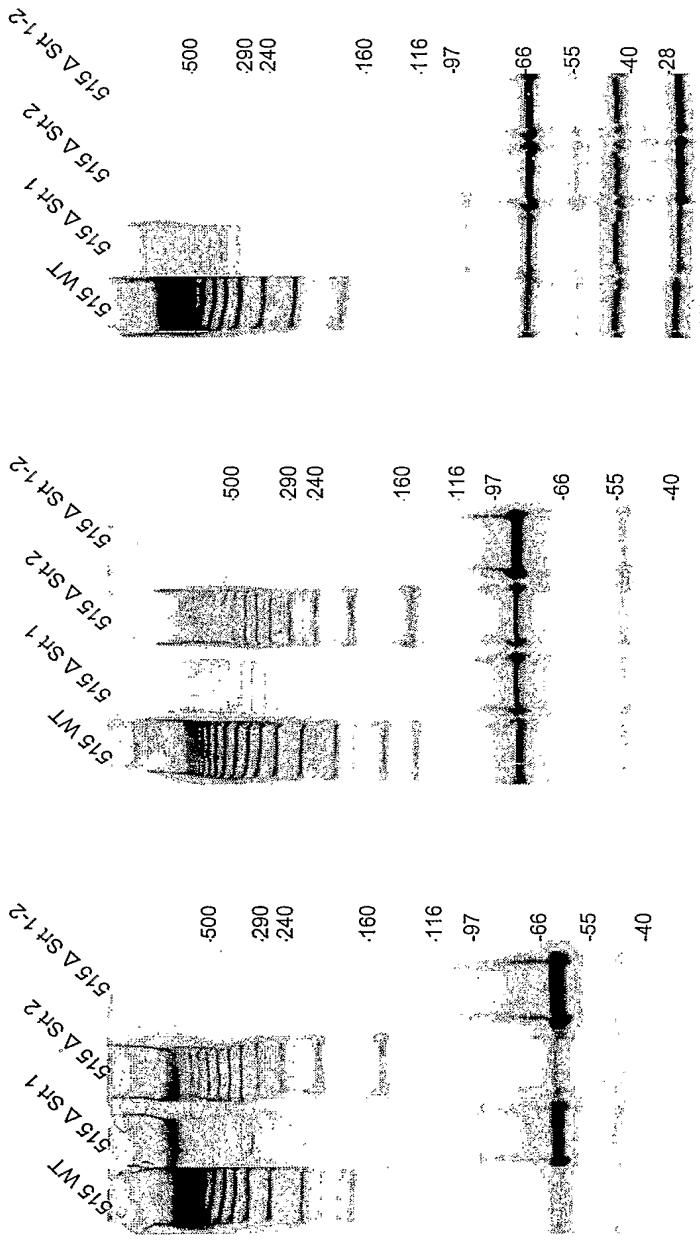
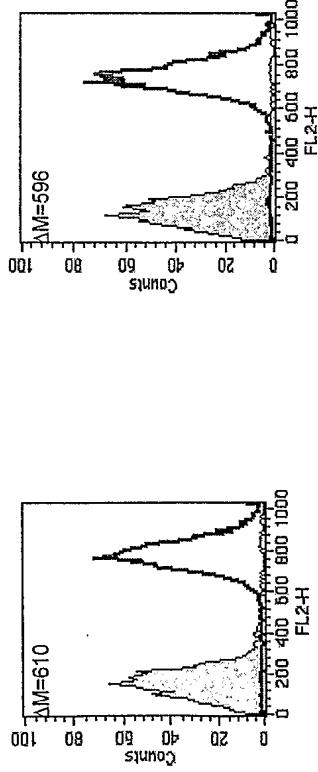
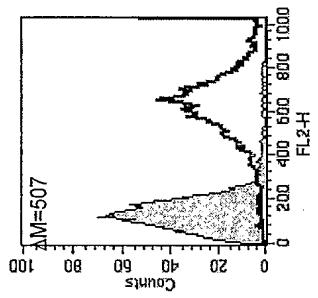
Figure 218

Figure 219

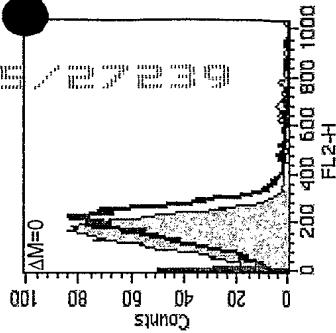
515 Δ Srt 1



515 Δ Srt 2



515 Δ Srt 3

 α^{59}

515 WT

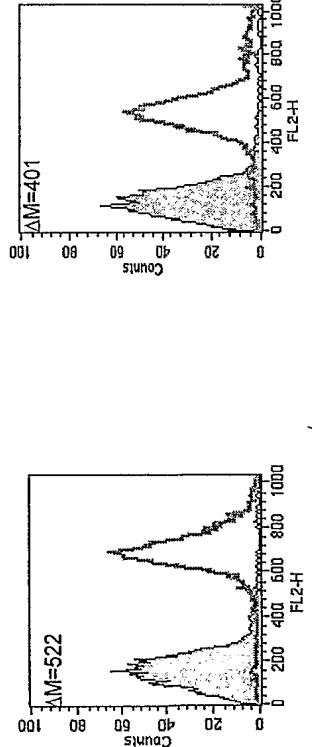
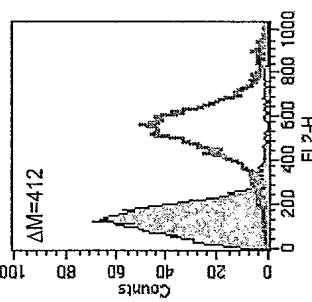
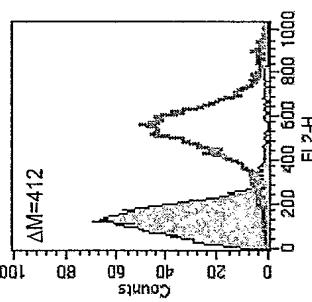
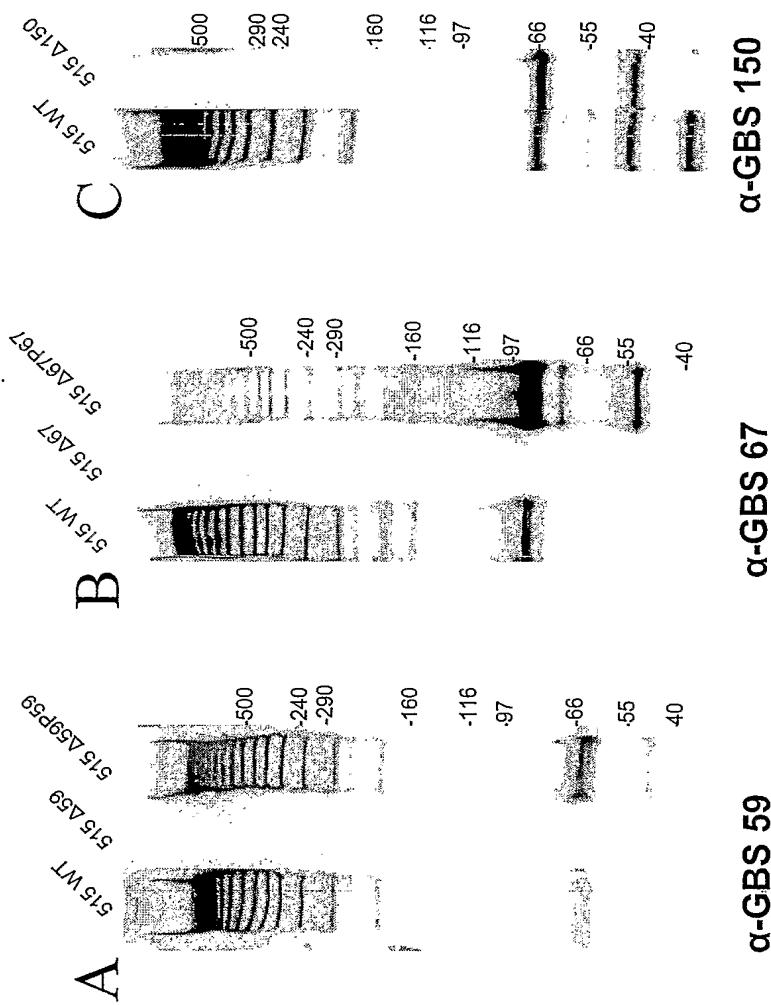
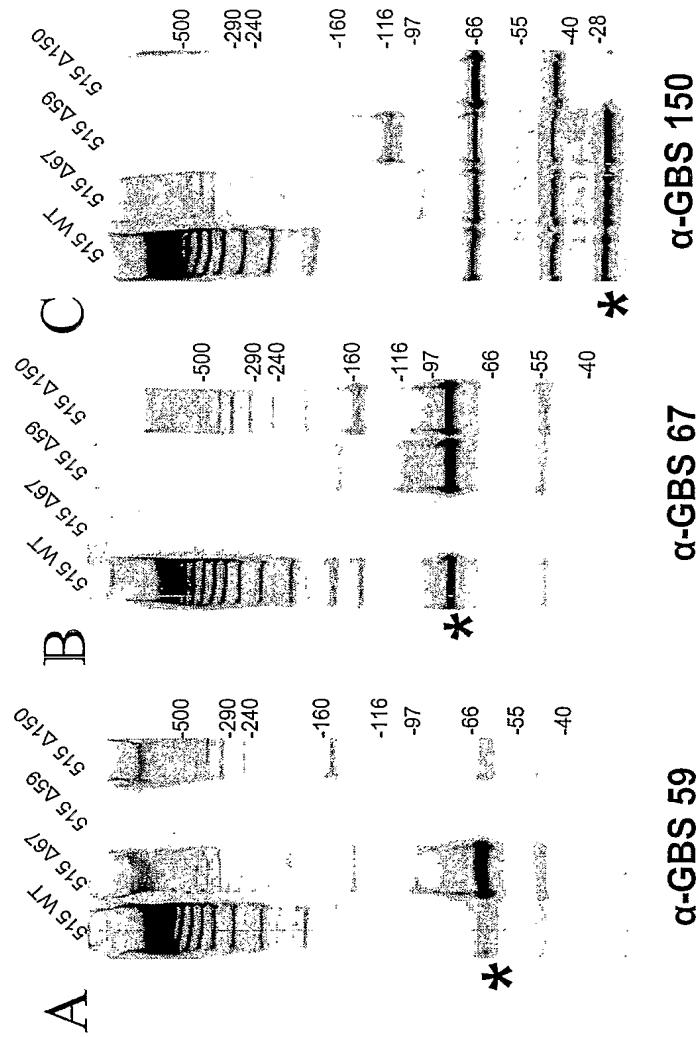
 α^{67} 

Figure 220

PCT/US05/27239 459/487

Figure 221

PCT/US05/27239

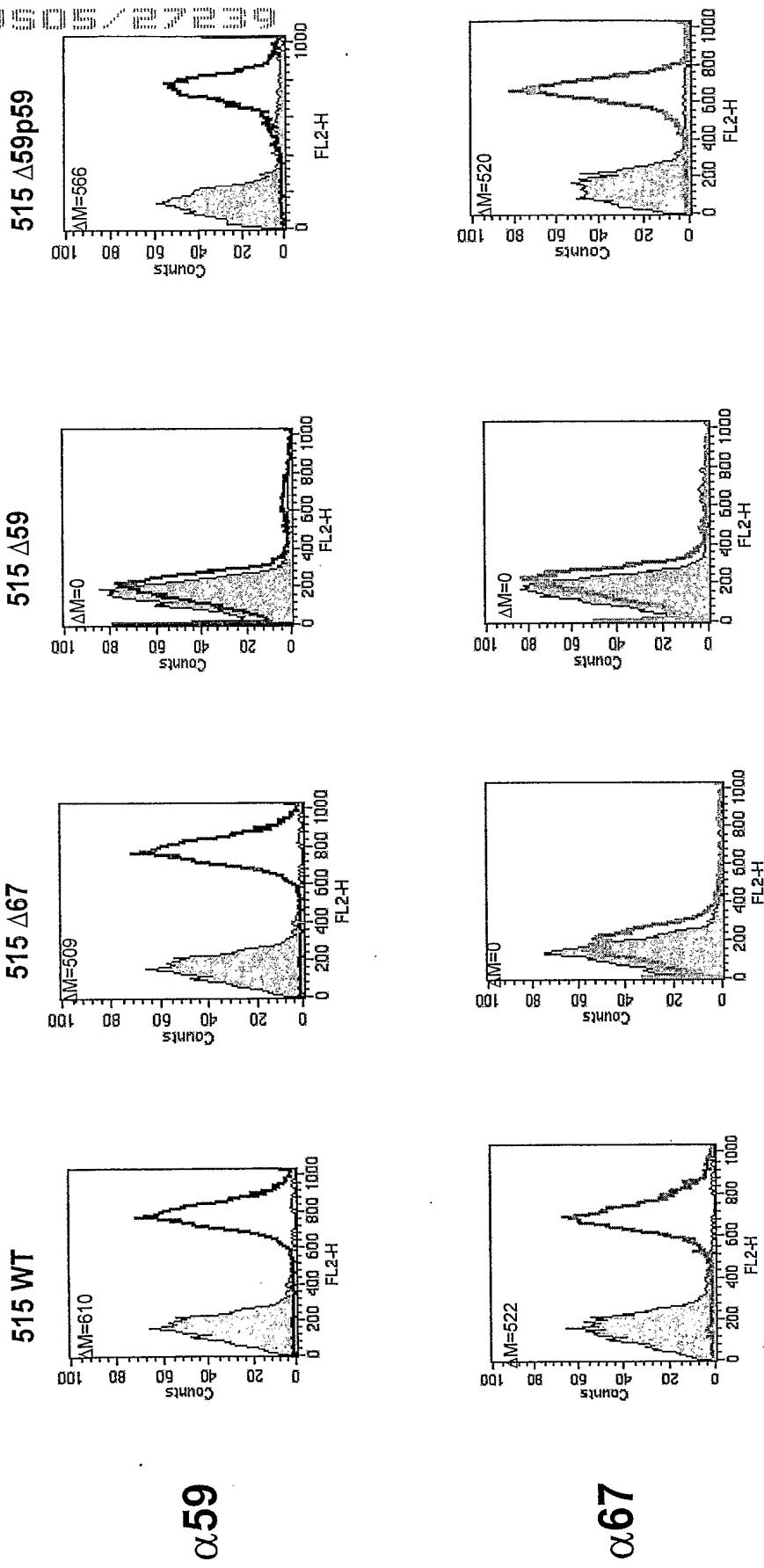
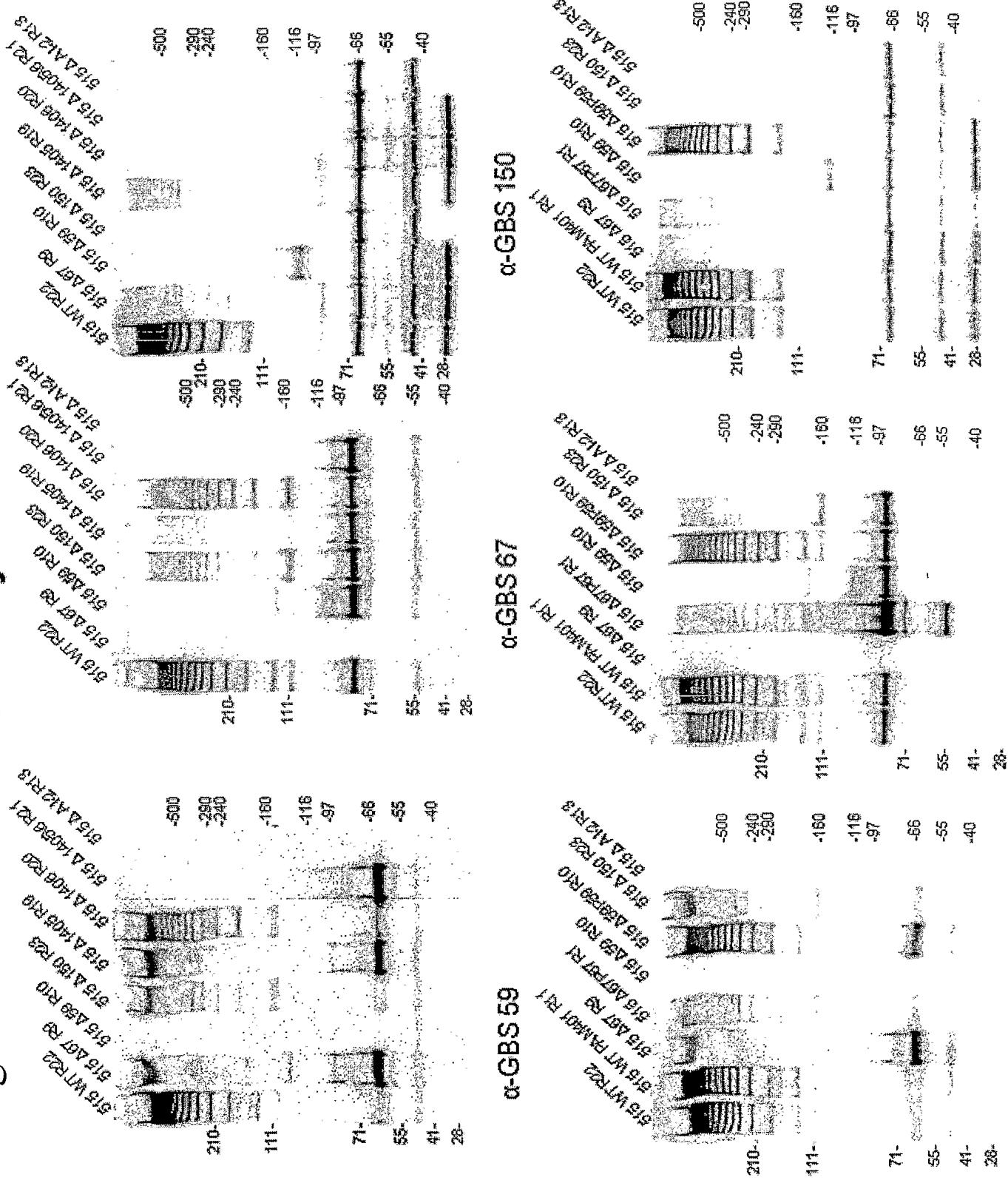
Figure 222

Figure 223

Summary WB



GBS 59 allelic variants

GBS strain % AA identity

7357b (Ib)	100
5518 (Ib)	100
5364 (V)	100
1999 (IV)	100
5408 (VIII)	98
coh31 (III)	98
d136c (III)	98
nem316 (III)	98

cjb111 (V)
674 aa

dk1 (Ia)	100
dk8 (Ia)	100
davis (Ia)	100
5551 (Ia)	100
2986 (Ia)	100
2110 (V)	100
2210 (IV)	100

515 (Ia)
675 aa

75%

48%

18RS21 (II)	100
3050 (II)	100
2141 (II)	100
1998 (III)	100
2928 (VII)	99,9

2603 (V)
705 aa

65%

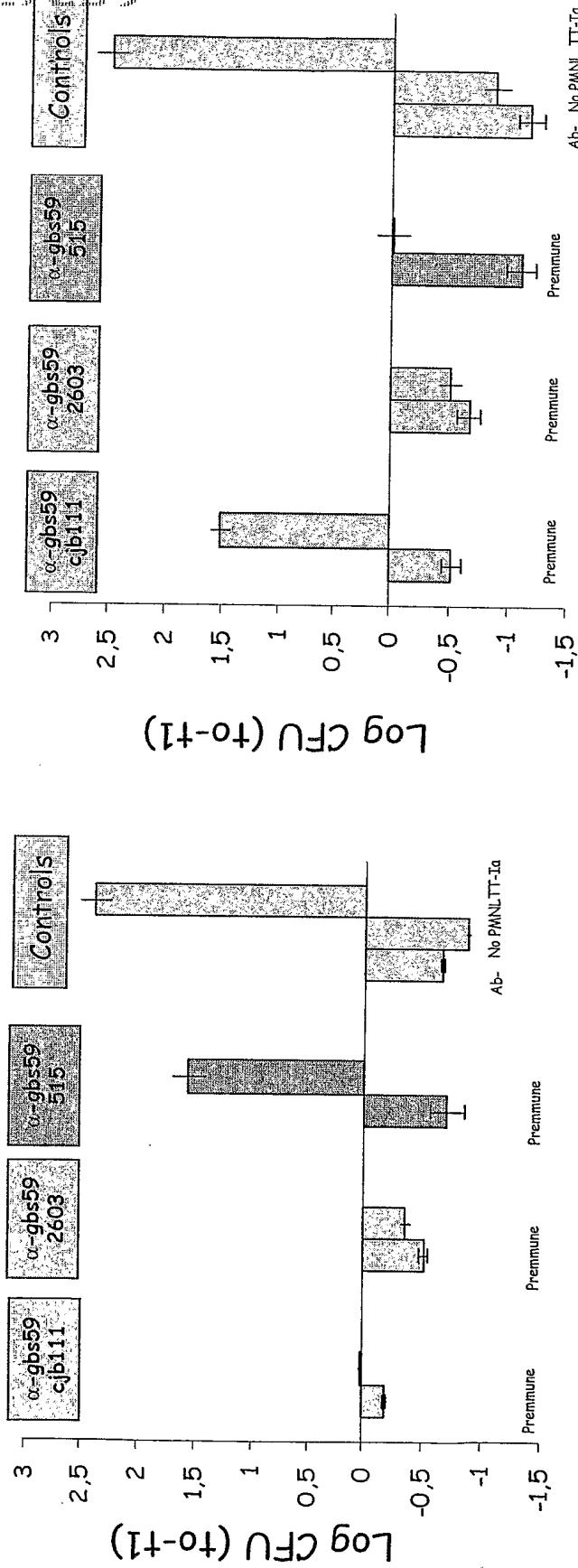
2274 (IV)	99,9
2129 (Ib)	99,7
5401 (II)	99,8

H36b (Ib)
693 aa

Figure 224

Figure 225

GBS 59 is opsonic only against homologous strain



- 515 (Ia) GBS strain

- cjb111 (V) GBS strain

Figure 226 A

		GBS 59		
GBS strains	Type	PCR	FACS (a-cjb111)	FACS (a-2603)
DK1	Ia	+	565	
DK8		+	559	
Davis		+	577	
515		+	583	0
090		+	0	0
2986		+	443	
5551		+	524	
H36B	Ib	+	0	410
7357b-		+	596	
5518		+	190	
D136C	III	+	504	
COH31		+	505	
1998		+	59	510
18RS21	II	+	0	353
DK21		+	249	0
3050		+	0	570
5401		+	0	400
2141		+	0	371
CJB111	V	+	625	0
2603		+	0	73
5364		+	593	
2110		+	590	0
2274	IV	+	0	400
1999		+	594	
2210		+	636	
5408	VIII	+	537	
CJB110	NT	+	0	0
1169		±	227	0

		GBS 59		
GBS strains	Type	PCR	FACS (a-cjb111)	FACS (a-2603)
A909	Ia	-	22	
2177	Ib	-	75	
COH1		-	0	0
M732		-	0	
M781	III	-	17	
5376		-	60	
5435		-	55	
SMU071		-	0	
JM9130013	VIII	-	0	0

Figure 226 B

Figure 227 A

GBS strains	Type	FACS (D Mean)				
		GBS 80	GBS 104	GBS 67	GBS 322	GBS 59
DK1	Ia	0	0	478	153	565
DK8		0	0	475	213	559
Davis		0	0	430	86	577
515		0	0	409	227	583
090		0	0	0	0	0
A909		46	29	0	0	0
2986		0	0	397	0	443
5551		0	0	485	36	524
2177	Ib	477	355	66	323	0
H36B		0	0	444	105	410
7357b-		91	0	316	102	596
5518		31	0	162	0	190
COH1	III	305	226	0	130	0
D136C		40	40	406	460	504
COH31		0	0	273	479	505
M732		141	101	0	292	0
M781		111	136	0	224	0
1998		140	77	350	288	510
5376		165	156	0	76	0
5435		93	100	0	88	0
18RS21	II	0	0	103	471	353
DK21		0	0	331	342	249
3050		71	46	460	188	570
5401		75	28	618	135	400
2141		0	0	370	76	371
CJB111	V	365	236	481	58	625
2603		62	0	105	293	73
5364		454	281	394	463	593

467/487

2110		0	0	589	0	590
2274		123	62	484	161	400
1999	IV	0	389	453	55	594
2210		0	0	574	0	636
SMU071		556	393	74	170	0
JM9130013	VIII	587	436	72	133	0
5408		0	0	433	0	537
CJB110	NT	0	0	245	587	0
1169		0	0	443	213	227
D Mean > 200		6/37 (16%)	7/37 (19%)	24/37 (65%)	14/37 (38%)	24/37 (65%)

Figure 227B

Figure 228

GBS Strain	Type	FACS (Δ Mean)										Δ mean	
		GBS 80 142-F		GBS 104 Mab		GBS 322 86		GBS 67 H36B		GBS 59 2603		GBS 59 515	
cdc-1	II	114	95	0	0	122	122	360	341	422	403	92	73
cdc-2	IB	173	69	92	0	95	75	552	448	590	486	135	31
cdc-3	II	566	508	360	302	85	60	364	306	433	375	111	53
cdc-4	V	524	432	337	245	284	204	577	485	625	533	105	13
cdc-5	II	140	0	0	0	462	300	487	297	563	373	175	0
cdc-6	V	544	484	361	301	95	95	586	526	601	541	55	0
cdc-7	III	155	116	44	5	134	118	95	56	138	99	74	35
cdc-8	III	347	304	192	149	74	62	98	55	170	127	72	29
cdc-9	II	89	65	0	0	226	191	390	366	504	480	181	157
cdc-10	IA	46	24	0	0	152	152	494	472	531	509	43	21
cdc-11	IA	17	0	0	0	295	135	569	550	569	550	47	28
cdc-12	V	439	430	290	281	60	30	174	165	227	218	52	43
cdc-13	IA	33	0	0	0	216	146	469	436	469	436	100	67
cdc-14	III	78	68	10	0	213	191	50	40	85	75	38	28
cdc-15	III	119	53	24	0	108	98	48	0	127	61	89	23
cdc-16	V	363	335	177	149	310	270	70	42	127	99	48	20
cdc-17	III	160	0	163	0	408	248	377	217	410	250	441	281
cdc-18	III	49	28	0	0	239	218	34	13	36	15	16	0
cdc-19	III	182	101	0	0	361	280	310	229	312	231	384	303
cdc-20	V	348	304	203	159	380	336	166	122	211	167	114	70
cdc-21	II	222	132	83	0	150	60	331	241	336	246	0	0
cdc-22	IA	0	0	13	13	43	43	238	238	238	238	43	43
cdc-22 (9-6-05)		23	0	34	0	110	20	310	220	320	230	113	23
cdc-23	V	484	484	374	374	278	278	124	124	206	206	11	11
cdc-24	V	137	52	0	0	333	248	90	5	110	25	110	25
cdc-25	IA	0	0	0	0	351	190	530	370	565	405	495	335
cdc-26	II	117	2	0	0	185	70	210	95	285	170	30	0
cdc-27	III	323	95	34	0	498	270	346	118	406	178	424	196
cdc-28	V	150	92	20	0	132	74	462	404	505	447	0	0
cdc-29	IV	90	73	65	48	195	178	90	73	150	133	150	133
cdc-30	V	390	187	336	133	348	145	229	26	244	41	113	0
cdc-31	IA	22	0	68	0	306	182	368	244	386	262	126	2
cdc-32	IA	45	0	12	0	260	175	190	105	205	120	30	0
cdc-33	II	50	0	0	0	306	156	134	0	237	87	4	0
cdc-34	III	152	60	47	0	342	250	44	0	74	0	27	0
cdc-35	V	227	227	40	40	246	246	395	395	415	415	0	0
cdc-36	IB	25	15	8	0	30	20	154	144	174	164	33	23
cdc-37	III	168	53	61	0	361	246	82	0	133	18	83	0
cdc-38	II	140	14	30	0	338	212	124	0	198	72	158	32
cdc-39	II	126	0	0	0	316	148	466	298	514	346	438	270
cdc-40	V	420	366	214	160	22	0	103	49	162	108	90	36
cdc-41	II	146	31	15	0	380	265	330	215	425	310	140	25

Figure 229

Expected strain coverage

MIX GBS proteins

vaccine options	w/o 59	w/o 322	w/o 104+322	w/o 59+322
n. antigens FACS+++	80+104+67+59+322	80+104+67+322	80+104+67+59	80+67+59
1	89%	89%	80%	80%
2	74%	51%	71%	64%
3	23%	14%	17%	16%

- GBS 322 but not GBS 59 is important to increase strain coverage
- GBS 59 probably could be useful to increase the vaccine strength

Assumption:

- Protein antigens that are highly accessible to antibodies confer 100% protection with suitable adjuvants

Figure 230

**GBS 59 opsonophagocytic activity is comparable
to that of the four-protein mix**

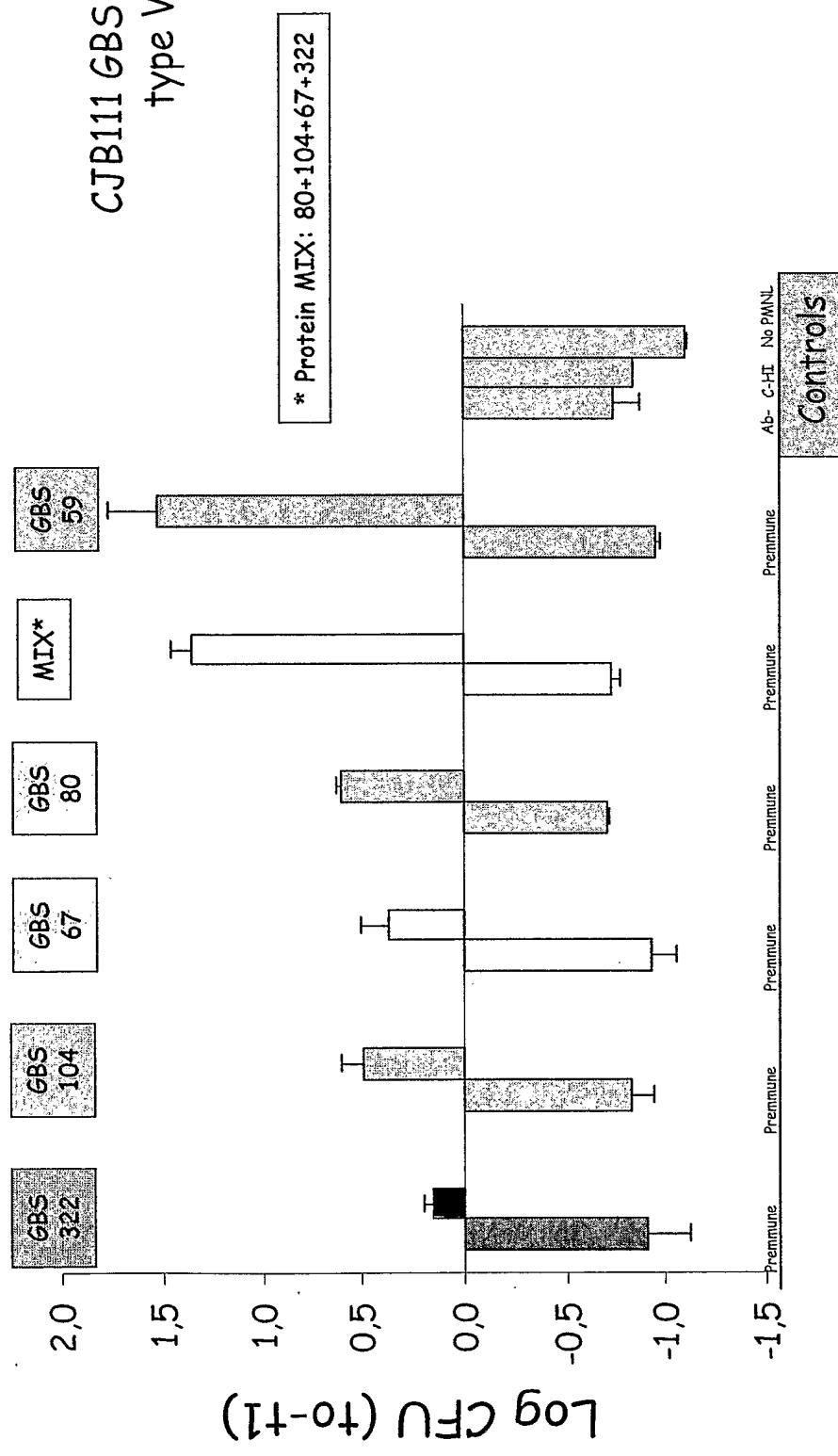


Figure 231

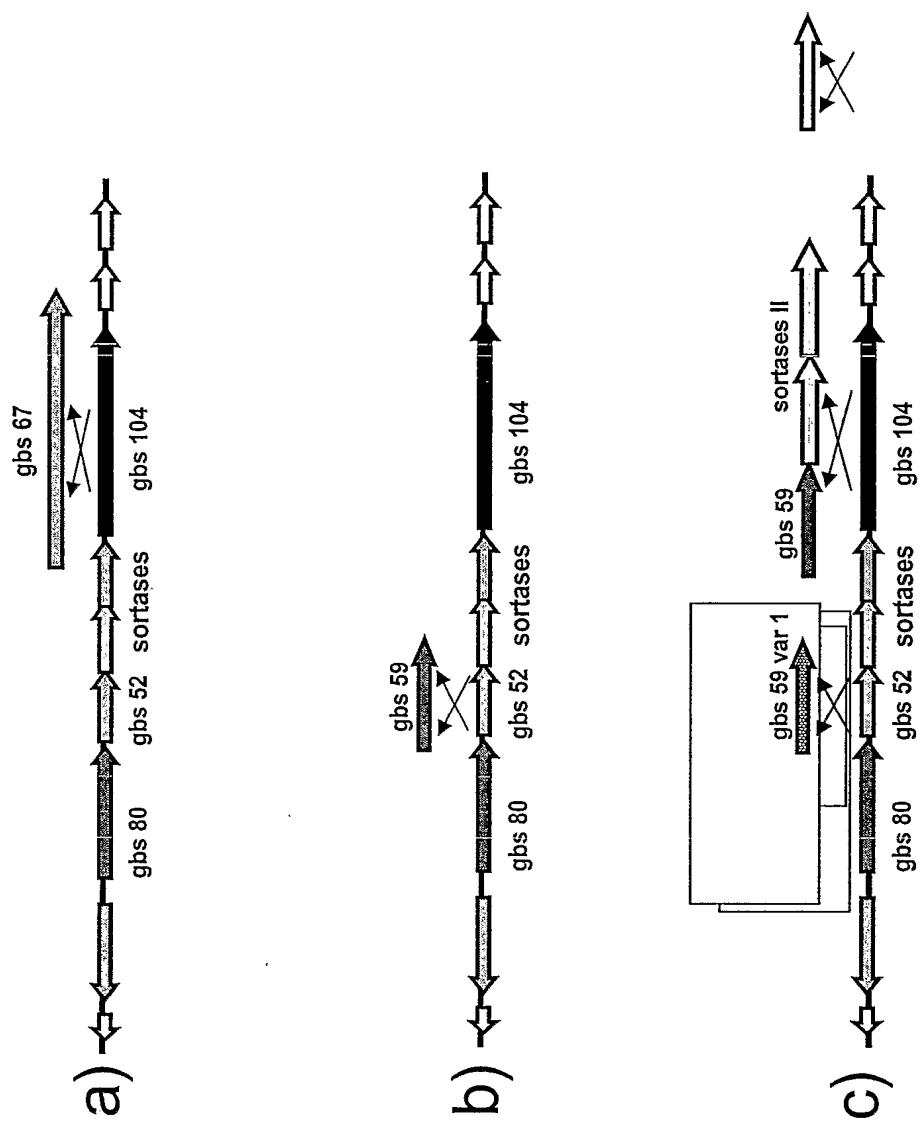
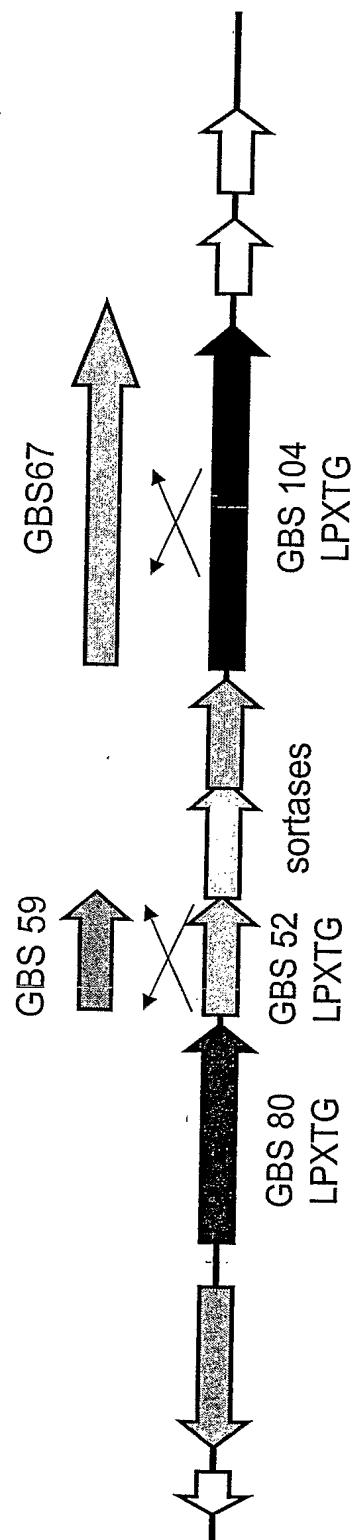
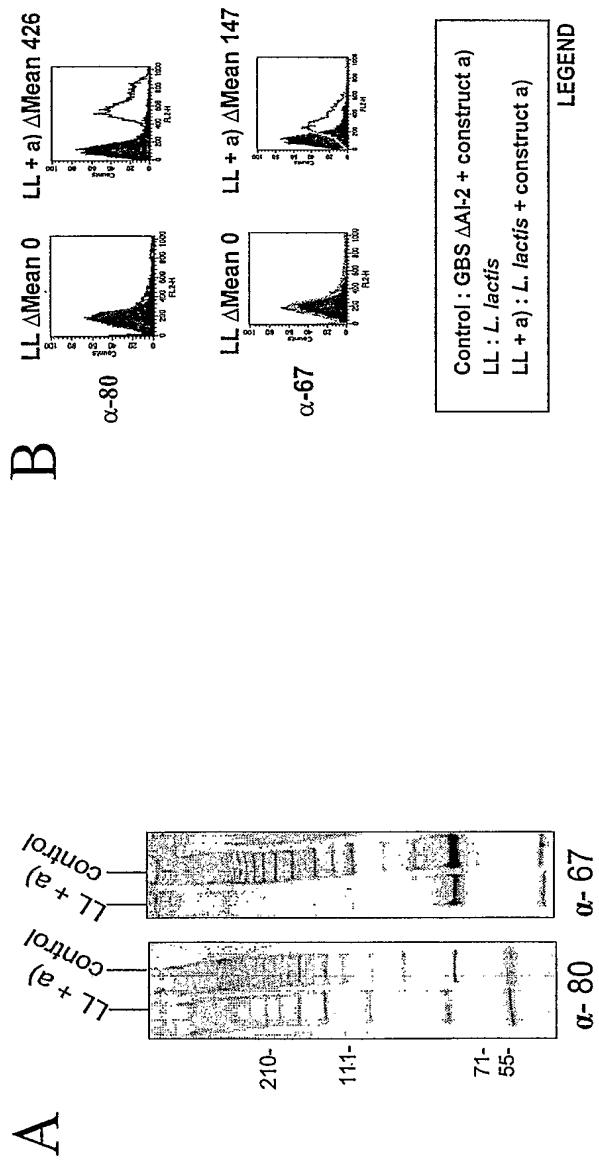


Figure 232



PCT/US05/27239 473/487

Figure 233

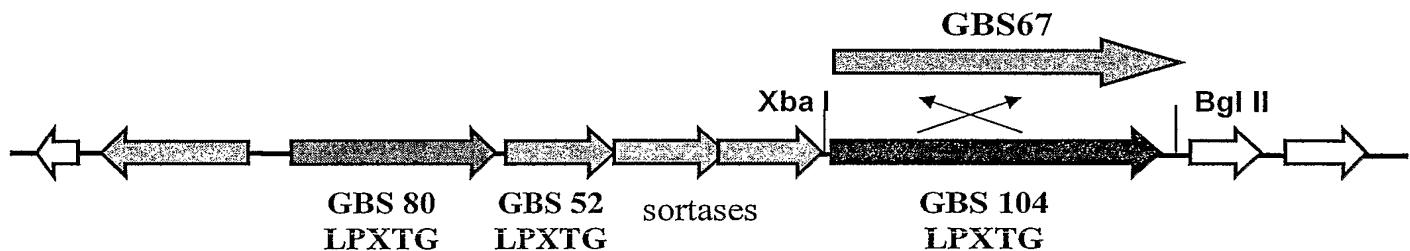


PCT/US05/27239 474/487

Figure 234 A

Introducing Heterologous Antigens into AI-1 pilus to Obtain Protection Across GBS Strains

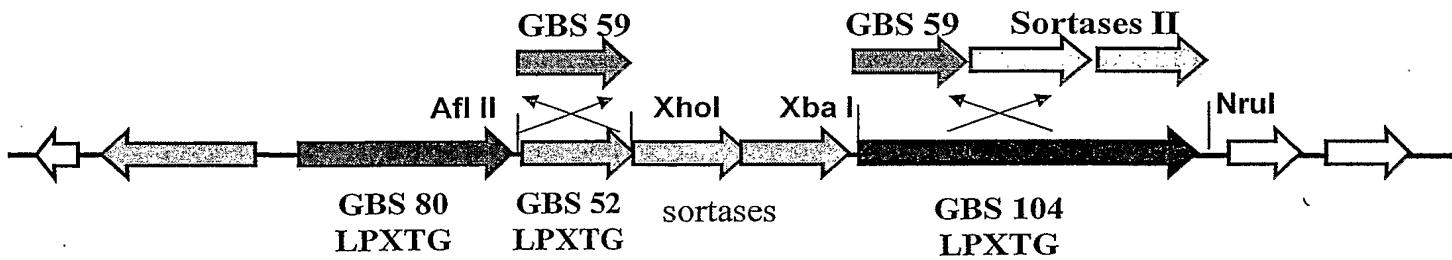
1- Substitution of GBS 104 with GBS67 from Island II



Oligo GBS67pAMXbafor AGTCAGTCTCTAGACGGCACAAATAGGAGTTGTAAA
 Oligo GBS67pAMBglrev CACCTGTCATAGATCTTAAGAATACTAAAGCGCATAA

2- Substitution of GBS52 or 104 with:

- GBS 59 alleles 515 or CJB
- GBS 59 allele CJB111 + sortases island II
- GBS 59 allele 515 + GBS 59 CJB111 + sortases island II



DETAILS:

a) Oligos to be used:

Oligo 59pAMAflfor1 AGTCAGTCCTTAAGCCGATATTATTAATCATGTTG (allele 515)

Oligo 59pAMAflfor1 AGTCAGTCCTCGAGTTAAACTTCCCTTGATTGACG (allele 515)

Oligo 59pAMAflfor2 AGTCAGTCCTTAAGAAGGAGTGGTGCTGCGGTAA (allele CJB111)

Oligo 59pAMXhorev2 AGTCAGTCCTCGAGTTAAGCTTCCCTGATTGACG (allele CJB111)

PCT/US2005/027239 475/487

b) Oligos to be used:

Oligo GBS59XbaF CTAGTGATATATCTAGAGAAAAAG

Oligo Sort59NruR CTAGCTAGTCGCGACTTTTCATTGGATTTCCCTTTC

Figure 234 B

3- Substitution of GBS104 with a fusion of GBS322-GBS67 to include GBS 322 into AI-1

- a) Construct 1: GBS67 complete sequence included
- b) Construct 2: Only part of GBS 67 was included (*deleted bold region*)

DETAILS:

a) Construct 1:

Legend:

Pink: GBS322

Black: GBS67

Black Bold: fragment of GBS67 eliminated in construct 2

Green PK motifs

Yellow E motifs

Red: LPXTG

> gbs67-515 + 322

```

MRKYQKFSKILTLSFCLSQIPLNTNVLGESTVPENGAKGLVVKKTDDQNKPLSKATFV
LKTTAHPESKIEKVTAELTGEATFDNLIPGDYTISEETAPEGYKKTNQTWQVKVESNGKT
TIQNSGDKNSTIGQNQEELDKQYPPTGIYEDTKESYKLEHVKGSVPNGKSEAKAVNPYSS
EGEHIREIPEGTLSKRISEVGDLAHNKYKIELTVSGKTIVKPVDKQKPLEIDTITIWTARTVSE
[ADLVKODNKSSYTVKYCDTLSSVISEAMSIDMNVLAKNNIADINLIYPETITHTYDQKSHTA
ISMKIETPATNAACOTTATVDLIKTNOVSVADOKVSLNTISEGMTPEAATTIVSPMKTYSSAT
ALKSKEVLAQEQAASCAAANEOVCPAPAVKSITSEVPAAKEEVKPTOTSVSQSTTVSPASV
AETPAPVAKVAPRTVAAPRVASVKVVTPKVETGASPEHVSAPAVTTTSPATDSKLOAI
EVKSVPAQQKAPTATPVAQPASTTNAVAAHPENAGLQPHVAAYKEIVASTYGVNEFSTYRAC
DPRDHGKGLAVDHVGTNOALGNKVAGMSTONMAANNISYVWQKEYSN
INSIGPANTWNAMPDRGGVTANHHDHVVSEN DVVFVLDNSS
MNNDGPNFQRHNKAKAAEALGTAVKDILGANSDNRVALVTYGSDIFDGRSVDVKGFKE
DDKYYGLQTKFTIQTENYSHKQLTNNAEEIIKRIPTEAPKAKWGSTTNGLTPEQQQKEYYL
SKVGETFTMKAFMEADDILSQVNRSQKIIVHVTDGVPTRSYAINNFKLGASYESQFEQM
KKNGYLNKSNFLLTDKPDDIKGNGESYFLPLDSYQTQIISGNLQKLHYLDLNLNYPKGII
IYRNGPVEHGTPTKLYINSLKQNYDIFNFGIDISGFRQVYNEEYKKNQDGTFQKLKEE

```

AFKLSDGEITELMRSFSSKPEYYTPIVTSADTSNNEILSKIQQQFETILTKENSIVNGTI
EDPMGDKINLQLGNGQILQPSDYTLQGNDGSVMKDGIA[REDACTED]GGPNNDGGILKGVKLEYIGNK
LYVRGLNLGEGQKVTLTYDVKLDDSFISNKFYDT[REDACTED]GRRTLNPKSED[PNTLRDFPIP]IRD
VREYPTITIKNEKKLGIEIEFIKVDKDNNKLLLKGATFELQEFNEDYKLYLPIKNNNSKVV
TGENGKISYKDLKGKYQLI[REDACTED]AVSPEDYQKITNKPILT[REDACTED]FEVVKGSIKNIIAVNKQISEYH
EEGDKHLITNTHIPPKGI[REDACTED]KGILSFILIGGAMMSIAGGIYIWKRYKKSSDMSIKK
D

Figure 234 C

b) Construct 2:

>gbs67-515 deleted+ 322

MRKYQKFSKILTLSFCLSQIPLNTNVLGESTVPENGAKGKLVVKKTDDQNKPLSKATFV
 LKTTAHPESKIEKVTAELTGEATFDNLIPGDYTSEETAPEGYKKTNQTWQVKVESNGKT
 TIQNSGDKNSTIGQNQEELDKQYPPTGIYEDTKESYKLEHVKGSPNGKSEAKAVNPYS
 SEGEHIREIPEGTLSKRISEVGDLAHNKYKIELTVSGKTIVKPVDKQKPLETDTTW
 IARTVSEVKADEVKQDNKSSYTVKYGDTLSMISFAMGIDMNVLAKINNIADINLYPETTTTV
 YMDOKSHITATSMNETPATNAACQITATVVDLKNOVSVADOKVSLNTDEGMITPEAATT
 VGRPMKTYSAFAKISKEYLAQEFDAVSQAAANEOMSPAPVKSITSEVPAKEEMKPTOTS
 VSCSTTVGFAGVANETPAFVAKVAPVRTVVAPRVVASMKVWVTPKVETGASPEHVSAPAVP
 VTTTTSPATDSKLQATEVKSMRVVAKARTATPVVQPASTTNAVAAHPENAGLOPHVVAAYK
 EKVAGSTYGVVNEFGTYRACDPDHGKGLAVDRIVGTINGAGNKVAOYSTQNMAANNNYW
 WQOKITYSNTNSIMGPANTWNAMPDRGGVTANHYDHVHVSHNKGESYFLFPLDSYQTQ
 IISGNLQKLHYLDLNLNYPKGIYRNGPVEHGPTKLYINSLKQKNYDIFNFGIDISGFRQ
 VYNEEYKKNQDGTFQKLKEEAFKLSDGEITELMRSFSSKPEYYTPIVTSADTSNNEILSKI
 QQQFETILTKENSIVNGTITIEDPMGDKINLQLGNGQILQPSDYTLQGNDGSVMKDGIATGG
 PNNDGGILKGVKLEYIGNKLYVRGLNLGEGQKVTLTVDKLDDSFISNKFYDTNGRTTL
 PSEDPNTLRDFPIPKIRDVREYPTTIKNEKKLGIEFIKVDKDNNKLLLKGATFELQEFNE
 DYKLYLPIKNNNSKVVTGENGKISYKDLKDGKYQLIFAVSPEDYQKITNKPILTFEVVKGS
 IKNIIAVNKQISEYHEEGDKHLITNTHIPPKGIKTCKGILSFILIGGAMMSIAGGIYIWKRY
 KKSSDMSIKKD

Oligos to be used:

Oligo GBS67pAMXbafor (vedi operone)

AGTCAGTCCTCTAGACGGCACAATAGGAGTTGTAA
XbaI

Oligo GBS67soe1rev

GAACGCGTAACTGTTTGTAACGGCTTTGTTGTCCACT

Oligo GBS322soe2for

GACAAACAAAAGCCGTTAGAAACAGAAGGACGGGGACAG

Oligo GBS322soe2rev1 (per costrutto non delete in 67)

GAGTACGAAGACAACATCTCTGAAATGATACGTTGAA

Oligo GBS322soe2rev2 (per costrutto delete in 67)

TAAAAAAGTAACCTCCCCTCTGTTAAATGATACGTTGAA

PCT/US05/27239 479/487

Oligo fine67soe3for1 (per costrutto non deleto in 67)~~CACGTATCATTTAACAAAGATGTTGTCTCGTACTCGAT~~**Oligo fine67soe3for2 (per costrutto non deleto in 67)**~~CACGTATCATTTAACAAAAGGGGAGAGTTACTTTTATTCC~~**Oligo GBS67pAMBgIrev (vedi operone)**~~CACCTGTCATAGATCTAAGAATACTAAAGCCATAAA~~

BgIII

PCT/US05/27239 480/487

Figure 234 D

PCR Soe1: GBS67pAMXbafor + GBS67soe1rev 727 bp

PCR Soe2 non del: GBS322soe2for + GBS322soe2rev1 1260 bp

PCR Soe2 del: GBS322soe2for + GBS322soe2rev2 1260 bp

PCR Soe3 non del: fine67soe3for1 + GBS67pAMBglrev 2061 bp

PCR Soe3 del: fine67soe3for2 + GBS67pAMBglrev 1419 bp

PCR Soe4 non del. PCR25: GBS67pAMXbafor + GBS67pAMBglrev 4000 bp

Substrato PCRSoe1, 2, 3 non del

PCR Soe4 del, PCR26: GBS67pAMXbafor + GBS67pAMBglrev 3312 bp

Substrato PCRSoe1, 2, 3 del

4- Substitution of GBS 52 with a fusion of GBS322-GBS52 to include GBS 322 into AI-1

(same legend as for GBS67 derivatives)

- a) Construct 1: GBS52 complete sequenze included
- b) Construct 2: Only part of GBS 52 was included (*deleted bold region*)

DETAILS:

a) Construct 1:

>GBS322-52 senza delezione di 52 (B) PCR 24

```

MKMNKKVLLTSTMAASLLSVASVQAQEIDITHEWIAITIVSEVKADLVKODNK
SSYTVKYGDTLISVISEAMSIDMNVIAKINNIADINIMPETTIITVTVDOX
SEITATSMKIELPATNAAGDTIATYDILKTNQMSVADOKVSIINTISFGMTPR
PAATTIVSPMKTFYSSAPALKSRREVLAQEGIAAVSGAAANEGUWSPA
RVKGITSEVPAAKEEVKPTOTSVSQSTTVSPASVAAETPAPVAKVAEVRIIVAAPRVA
VKVVTFRKVETGASPEHVGARAVPVTTTSPATDSKLOATEVKSPVVAOKAF
TATPVACOPASTTNAVAAHPEAQLCOPHVAAYKEKVAESTYGVNEFSTYRAG
DPGDHIGKGIAVDIFIVGTNQALGNKVAQYSTONMAANNISYYIWQOKKEYSN
TNSIYGPANTWNAMPDRGGVITANHYDHVHYSFNH HQLTIVHLEARIDRPNPQL
EIAPKEGTPIEGVLYQLYQLKSTEDGDLLAHWNSLTITELKQAAQQVFEA
TTNQQGKATFNQLPDGIYYGLAVKAGEKNRNVSAFLVLDLSEDKVYIPKII
WSTGELDLLAVGVDGDTKKPLAGVVFELYEKNGRTPIRVKNGVHSQDIDA
AKHLETDSSGHIRISGLIHGDYVVLKEIETQSGYQIGQAETAVTIEKSKT

```

WO 2006/078318

PCT/US05/27239 481/487

PCT/US2005/027239

TVTIENKKVPTPKVPSRGGL [REDACTED] QQAMALVIIGGILIALRLLSKH
RKHQNKD

PCT/X-2005/22239

482/487

Figure 234 E

b) Construct 2:

>GBS322-52 (A) PCR 23

MKMNKKVLLTSTMASLLSVASVQAQETDTITWTARTVSEVKADLVKODNK
SSYIVKYGDTLSVISEAMSIOMNVYLAKINNIADINLYPETTLTVTYDOK
SHTATSMKIEITPATNAACQDTATVDEIKTNQSVADOKVSLNTSEGMTPE
VATTIVSPFMKTYSSAPALKCKEVLAOEQAQAVSCAAAANEQVSPA
PVKSITSEVPAAKEEVKFTOTSVSOSTITVSPAGVAAETPATPVAKVAPVRVMAAPRVAS
VAKMVTPKMETGASPEHNSAPAVPVTTTSPATDSKLOATEVKSPVPAQKAH
IATPVACOPASTTNAVAAHPENAGLOPHVAAYKEKVASTYCVNEFSTYRAG
DPGDHGKGIAVMDHMGTNGALGNKVAQYSTONMAANNISYMWQOKEFYSN
INSIXGPANTWNAMPDRGCVTANHYDHMVMSFNK
QGKATFNQLPDGIYYGLAVKAGEKNRNVSAFLVDLSEDKVIYPKII
WSTGELDLLKVGVDGDTKKPLAGVVFELYEKNGRTPIRVKNGVHSQDIDA
AKHLETDSSGHIRISGLIHDGYVILKEIETQSGYQIGQAETAVTIEKSKT
TVTIENKKVPTPKVPSRGGLPKCQQAMALVIIGGILIALALRLLSKH
RKHQNKD

Oligos to be used:

Oligo 322Aflfor1

AGTCAGTCCTAAGGATATTATAGTCTCGGACTA

Af 11

Oligo 52 soe1 forA

CAAGGAAAGGCTACATTTAACCC

Oligo 52 soe1 forB

TCGACCTTCAATTAAACAAACATCAGTTGACGATTGTTCATC

Oligo52 soe1revA

AAATGTAGCCTTCCTTG TTG TAAATGATACCGTGAACC

Oligo52 soe1revB

AACAATCGTCAACTGATGTTCTTAATGATAACGTGAAGC

Oligo 52Xhorev

AAGACCTCCTCGAGATGGCACTT

PCT/US05/27239

483/487

Xho I

PCR Soe1A: Oligo 322Aflfor1+ Oligo 52 soe1 revA 1370 bp

PCR Soe2A: Oligo 52 soe1forA + Oligo 52Xhorev 520 bp

PCR Soe3A: Oligo 322Aflfor1 + Oligo 52Xhorev 1846 bp (con PCR Soe1A + PCR Soe2A)
(PCR23)

PCR Soe1B: Oligo 322Aflfor1+ Oligo 52 soe1 revB 1370 bp

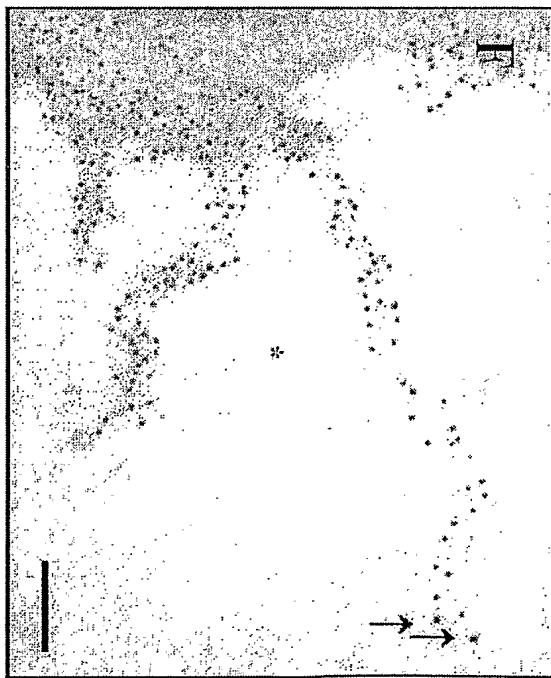
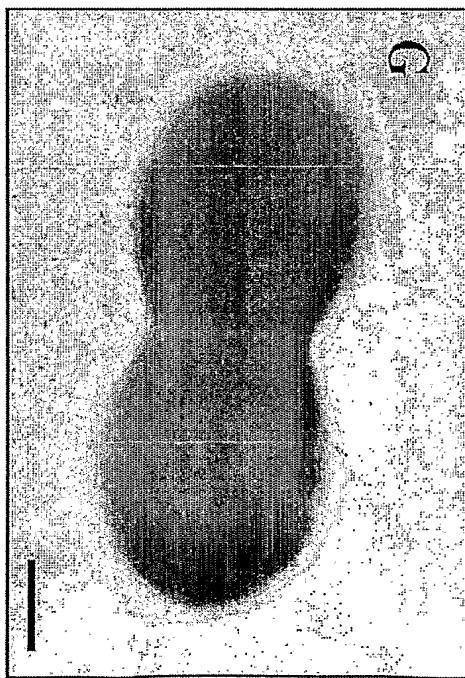
PCR Soe2B: Oligo 52 soe2forB + Oligo 52Xhorev 742 bp

PCR Soe3B: Oligo 322Aflfor1 + Oligo 52Xhorev 2068 bp (con PCR Soe1B + PCR Soe2B)
(PCR 24)

484/487

Figure 235

Figure 236



Strain variability - GBS67: 2 alleles

Differences between strains		2603 and H36B	(AA not matching/AA total and % of homology)	114 / 828 (87.1%)
1	MRKYQKFSKILLTSLFCISQIPINTVNLGESTVPENGAKGLVKKKTDDQNVLGESTVPENGAKGLVKKKTDDQ	25	451 PLDSYQTOIIISGNLQLKLHYDLNNNYPKGTTIRNGPYKEHGTPTKLYINS 500 NVLGESTVPENGAKGLVKKKTDDQ
51	NKPLSKATFVLLKTTAHPESKIEKVTAELTGATEFDNLIPGDTILSEETAP	100		421 PLDSYQTOIIISGNLQLKLHYDLNNNYPKGTTIRNGPYREHGTPTKLYINS 450 NVLGESTVPENGAKGLVKKKTDDQ
26	NKPLSKATFVLLKPTSHSESSEKVKVTVTGTGATEFDNLIPGDTILSEETAP	75		501 LKQKNYDIFNFGIDISGFRQVYNEEYKKNQDGTFQKLKEEAFKLSDGEIT 550 NVLGESTVPENGAKGLVKKKTDDQ
101	EGYKKTNTWQVKVESNGKTTIIONSGDKNSTIGONQEELDKQYPPGTGIE	150		471 LKQKNYDIFNFGIDISGFRQVYNEDYKKNQDGTFQKLKEEAFKLSDGEIT 520 NVLGESTVPENGAKGLVKKKTDDQ
76	EGYKKTNTWQVKVESNGKTTIIONSGDKNSTIGONQEELDKQYPLTGAIE	125		551 EIMRSFSSKPEYYTPIVTSADTSNEILSISKIOQQETFLIKENSTVNGTI 580 NVLGESTVPENGAKGLVKKKTDDQ
151	DTKESYKLEHVKGSPNGKSEAKAVNPYSSSEGHEIREIPEGTLSKRISEV	200		521 EIMNSFSSKPEYYTPIVTSADVSNEILSISKIOQQFERKLTKENSTVNGTI 540 NVLGESTVPENGAKGLVKKKTDDQ
126	DTKESYKLEHVKNSTIPNGKLEAKAVNPYSSSEGHEIREIPEGTLSKRISEV	175		601 EDPMGDKINLHQINGQTLQPSDYLQGNDGSTMKDGIAATGGPNNDGGILK 650 NVLGESTVPENGAKGLVKKKTDDQ
201	GDLAIRNKYKTELTIVSGKTCIVKVDKQKPLDVFVLDNSNSMNDGPNEQR	250		571 EDPMGDKINLHQINGQTLQPSDYLQGNDGSTMKDSIATGGPNNDGGILK 620 NVLGESTVPENGAKGLVKKKTDDQ
176	NDLDHENKYKTELTIVSGKSTIKTINKDEPLDVVFVLDNSNSMNRNGKN ...	222		651 GYKLEYIGNKLYVRGLNLGEGRQVTLTDVKLDDSFISNKFYDNGRTTL 700 NVLGESTVPENGAKGLVKKKTDDQ
251	HNKAKKAAEALGTAVKDILGANSDNRVALTYGSDFEDGRSVVVKGKE	300		621 GYKLEYIGNKLYVRGLNLGEGRQVTLTDVKLDDSFISNKFYDNGRTTL 670 NVLGESTVPENGAKGLVKKKTDDQ
223	NCIAKSAEAEVETIKDVLGANVENRAALTYGSDFEDGRTVKVKLGKE	271		701 NPKSEDPNTLRDEPIPKIRDVREYPTITIKNEKKGEIEFKVDKDNKKL 750 NVLGESTVPENGAKGLVKKKTDDQ
301	DDKYGLOETKFTQTONENYSKQQLTNNAEETIKRIPTEAKKGSTTNGL	350		671 NPKSEEPDTLDEPIPKIRDVREYPTITIKNEKKGEIEFKVDKDNKKL 720 NVLGESTVPENGAKGLVKKKTDDQ
272	DPTYGLETSFTYQTNDSYKCFETNTAADLTKPKEAPEAKNGCTSLGL	320		751 LIKGATEFELQEFNEDYKLYPLKNNNSKVTGENGKISYKDLKGKYQLI 800 NVLGESTVPENGAKGLVKKKTDDQ
351	TPEQKEYLISKVGETETMKAMEADDILSQVNRSQKLIVHEDGYPTR	400		721 LIKGATEFELQEFNEDYKLYPLKNNNSKVTGENGKISYKDLKGKYQLI 770 NVLGESTVPENGAKGLVKKKTDDQ
321	TPEKEREXDLSKVGTEETMKAMEADTLSSIQERSKRLIVHEDGYPTR	370		801 EA5PEDYQKITNKPILTEVVVKGSKNNIAVNQKISEYHEEGDKHLITN 850 NVLGESTVPENGAKGLVKKKTDDQ
401	SYAINNFKUGAESTESOFOQMKGNGLINKSNFLTDKPEDIKRGGESEYLF	450		771 EA5SPKDQKITNKPILTEVVVKGSQNIIAVNQKISEYHEEGDKHLITN 820 NVLGESTVPENGAKGLVKKKTDDQ
371	SYAINSFVKGSTANOFFERIKRGYLDKNNYFTDPERIKRGGESEYLF	420		851 THIPPKGI.....NVLGESTVPENGAKGLVKKKTDDQ

Strain variability - GBS67 Allele I (2603)

WO 2006/078318

PCT/US05/27239

486/487

PCT/US2005/027239

Strain	Differences in comparison with 2603 (% of homology)
2603	-
18RS21	1/833 (99.9%)
CJB111	14/833 (98.3%)
515	2/833(99.8%)

Figure 238

Strain variability - GBS67

Allele II (H36b)

WO 2006/078318
PCT/US2005/027239

487/487

PCT/US2005/027239

Strain	Differences in comparison with H36b (% of homology)	FACS (α -67 from 2603)
H36B	-	444
1169	10/823 (98.8%)	443
090	9/316	0
CJB110	11/824 (98.7%)	245

Figure 239

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
27 July 2006 (27.07.2006)

PCT

(10) International Publication Number
WO 2006/078318 A3

(51) International Patent Classification:
A61K 39/02 (2006.01)

I-53100 Siena (IT). **RINAUDO, Daniela** [IT/IT]; CHIRON VACCINES, 1, Via Fiorentina, I-53100 Siena (IT). **MASIGNANI, Vega** [IT/IT]; CHIRON VACCINES, 1, Via Fiorentina, I-53100 Siena (IT). **BAROCCHI, Michelle** [IT/IT]; CHIRON VACCINES, 1, Via Fiorentina, I-53100 Siena (IT). **RAPPULOI, Rino** [IT/IT]; CHIRON VACCINES, 1, Via Fiorentina, I-53100 Siena (IT).

(21) International Application Number:
PCT/US2005/027239

(22) International Filing Date: 29 July 2005 (29.07.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/592,805	29 July 2004 (29.07.2004)	US
60/609,833	13 September 2004 (13.09.2004)	US
60/616,833	8 October 2004 (08.10.2004)	US
60/633,418	7 December 2004 (07.12.2004)	US
60/640,069	30 December 2004 (30.12.2004)	US
60/660,321	11 March 2005 (11.03.2005)	US
60/673,754	22 April 2005 (22.04.2005)	US
60/693,001	21 June 2005 (21.06.2005)	US
60/695,453	1 July 2005 (01.07.2005)	US
60/697,643	11 July 2005 (11.07.2005)	US

(74) Agent: **HALE, Rebecca, M.**; Novartis Vaccines and Diagnostics Inc., P.O. Box 8097, Emeryville, CA 94662-8097 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
30 October 2008

(54) Title: IMMUNOGENIC COMPOSITIONS FOR GRAM POSITIVE BACTERIA SUCH AS STREPTOCOCCUS AGALACTIAE

(57) Abstract: The invention relates to the identification of a new adhesin islands within the genomes of several Group A and Group B Streptococcus serotypes and isolates. The adhesin islands are thought to encode surface proteins which are important in the bacteria's virulence. Thus, the adhesin island proteins of the invention may be used in immunogenic compositions for prophylactic or therapeutic immunization against GAS or GBS infection. For example, the invention may include an immunogenic composition comprising one or more of the discovered adhesin island proteins.

WO 2006/078318 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/27239

A. CLASSIFICATION OF SUBJECT MATTER

IPC: A61K 39/02(2006.01)

USPC: 424/190.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/190.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
MEDLINE, BIOSIS, HCPLUS, EMBASE, DERWENT, PUBLISHED APPLICATIONS AND ISSUED PATENTS.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/34771 A2 (TELFORD et al) 02 May 2002 (02.05.2002), see pages 1411 and 3057. (only the relevant pages provided)	1-7 and 17-24
X	LARSSON et al. Protection against experimental infection with group B streptococcus by immunization with a bivalent protein vaccine. Vaccine. February 1999, Vol. 17, No. 5, pages 454-458.	1-7 and 17-24

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier application or patent published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means		
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

21 May 2008 (21.05.2008)

Date of mailing of the international search report

25 AUG 2008

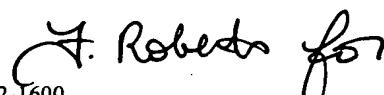
Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
Facsimile No. (571) 273-3201

Authorized officer

PADMA v. BASKAR

Telephone No. 571-272-1600



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/27239

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.: 1-7 and 17-24

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

<input type="checkbox"/>	The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
<input type="checkbox"/>	The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
<input type="checkbox"/>	No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US05/27239

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

1. This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim 1 -7 (in part) drawn to an immunogenic composition comprising a purified Group B Streptococcus adhesion island polypeptide.

Further species election to one composition comprising GBS AI -1 or GBS AI -2 required (see paragraph # 3).

Group II, claims 8-16 (in part) drawn to an immunogenic composition comprising a purified gram positive adhesion island polypeptide.

Further species election to one composition comprising one bacteria and one GAS AI -1 ,GAS AI -2,GAS AI -3 and GAS AI -4 required (see paragraph # 3).

Group III, claims 17-24 (in part) drawn to an immunogenic composition comprising a first and second purified Group B Streptococcus adhesion island polypeptide.

Further species election to one combination of first and second polypeptide (see paragraph # 3).

Group IV, claims 25-34 (in part)drawn to an immunogenic composition comprising a first and second gram positive GAS AI -adhesion island polypeptide.

Further species election to one combination of first and second polypeptide (see paragraph # 3).

Group V, claims 35-39 and 40 (in part)drawn to a modified gram positive bacterium and a method of manufacturing adhesion island antigen

Further species election to one modified gram positive bacterium required (see paragraph # 3).

Group I is directed to an immunogenic composition comprising polypeptide GBS AI -1 or GBS AI -2 whereas Group II is drawn to immunogenic composition comprising gram positive bacterial adhesion polypeptides GAS AI -1 , GAS AI -2 , GAS AI -3 and GAS AI -4 . These inventions are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1 because these two compositions do not share a common structure ,property and function as group I contains GBS polypeptide where as group II comprises GAS polypeptides . Group III and Group IV are also drawn to compositions as group III comprises combination of two polypeptides from GBS that shares no common structure ,property and function with Group IV as it comprises GAS polypeptide and thus do not share a single inventive concept. Thus these inventions are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1 Group V is drawn to a modified bacterium from GBS , GAS and non-pathogenic gram positive bacterium comprising expressing polypeptide GBS- AI -1or GBS-AI-2 and not share a single inventive concept from other four groups as the composition contains polypeptides which does not share a common structure, property and function.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US05/27239

2. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

3 Group I species: GBS AI -1 80, 104, 52, 59, 67, 150, 01521, 01523, 01524 or GBS AI -2

Group II species: GAS AI -1 , GAS AI -2 , GAS AI -3 and GAS AI -4.

Group III species: Any combination of first and second polypeptide from GBS AI -1 80, 104, 52, 59, 67, 150, 01521, 01523, 01524, GBS AI -2.

Group IV species: Any combination of first and second polypeptide from GAS AI -1 , GAS AI -2 , GAS AI -3 and GAS AI -4

Group V species : Modified gram-positive bacterium or non pathogenic bacterium expressing GBS AI -1 80, 104, 52, 59, 67, 150, 01521, 01523, 01524, GBS AI -2 , GAS AI -1 , GAS AI -2 , GAS AI -3 and GAS AI -4

The inventions listed as Groups 1-5 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The technical feature of linking groups appears to be that they are all related to immunogenic compositions comprising adhesion peptides methods of making adhesion peptide.

However, Beckmann et al Infection and Immunity, June 2002, p. 2869-2876, Vol. 70, No. 6 disclose an immunogenic composition comprising adhesion oligomeric polypeptide (see page 2871, left column last paragraph through right column and figure 3) As this polypeptide binds to fibrinogen it is an adhesion immunogen. Therefore, the technical feature of linking groups 1-5 does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art and hence unity of invention is lacking.

The special technical feature of Groups 1-5 is considered to be immunogenic compositions comprising polypeptides that share no common structure, property and function and thus do not share the same or a corresponding technical feature .

Accordingly, Groups 1-5 are not so linked by the same or a corresponding special technical feature as to form a single general inventive concept.

The claimed species GBS AI -1 80, 104, 52, 59, 67, 150, 01521, 01523, 01524, GBS AI -2 ; GAS AI -1 , GAS AI -2 , GAS AI -3 and GAS AI -4 have no common structure and thus are not linked by the same or a corresponding special technical feature so as to form a single general inventive concept under Rule 13.1. Hence, unity is lacking among species.